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Factors associated with poor memory functioning in persons with epilepsy.

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FACTORS ASSOCIATED WITH POOR MEMORY FUNCTIONING IN PERSONS WITH EPILEPSY

by

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Abstract

A multifactorial approach was used to investigate factors that were expected to be significant correlates of poor memory functioning in persons with epilepsy. The relationships between side of temporal lobe (TL) seizure focus, duration of epilepsy, Boston Naming Test (BNT) score, anxiety, and depression, and memory in the verbal and visual-spatial domains, were evaluated in 142 epilepsy surgery candidates. In general, the results indicated that, (1) as a group, persons with epilepsy displayed lower than average delayed memory test scores, (2) side of TL seizure focus predicted verbal memory score but not visual-spatial memory score, and (3) BNT score, anxiety, and age or duration predicted visual-spatial memory score but not verbal memory score. The results were discussed in the context of a model of hemispheric specialization based on differences in neuronal organization (Goldberg & Costa, 1981). Within this model, verbal and visual-spatial memory test demands were re-examined in terms of the nature of the test stimuli within each modality.

Acknowledgments

Ah, finally, the acknowledgments. It seems somewhat of an anomaly that this section should come at the beginning of this document, when it is certainly the section written last. Beware, I plan to take full advantage of the lack of style or format restrictions here. If you think this is not the place for candour, turn the page now.

Anyone who has had to pour a limited supply of creative energy into an immense project, working alone in a small room, with the aim of producing a written document for public scrutiny, without a sufficient preparatory experience, knows that it cannot be completed without many, many, individuals who assist along the way in direct and indirect ways. More people than I will mention here have provided assistance, favours, moral support, a place to stay, kind words, gently-applied pressure, criticism, and many more nouns than my finite brain can generate.

My first acknowledgement must go to my husband Geoff Haddock (also a doctor he reminds me) who, way back in 1988, set an example of what it can be like to be an undergraduate student who wants to succeed. Next, I'd like to mention Prof. Morris Moscovitch, whose innocent question "Have you applied to any graduate schools yet?" had an remarkable effect on me. One must be careful what one says to drifting research assistants. Next, I should thank whoever decided to accept me into the University of Windsor Clinical Neuropsychology Programme.

Okay, okay, my reminiscences must be boring you. Let's fast-forward to those persons involved with helping me along with my PhD project. I'd like to thank the staff in the Neuropsychology Division at Henry Ford Hospital, most notably Dr. John Fisk, June Blackwell, and Sandy Scott for guidance and many favours, and Drs. Brien Smith, Ken Podell, and Mark Lovell for allowing me access to their patient files. I hope we have all benefitted from my toils. Of course, I'd like to thank my committee members, Drs.

Douglas Shore, John Fisk, Patricia Weir, and Prof. Byron Rourke. They had to put up with the fact that I lived England during the entire writing process, which often made communication rather inconvenient. I am grateful for their comments, especially at the proposal meeting (at which point it was obvious that I could use some treatment for my sense-of-direction disability). Thank you to my external-examiner Dr. Marilyn Jones-Gotman of McGill University, for apt comments.

This project would never have seen the light of day without Geoff's irritating whip-cracking. Also, he was always ready with editorial and statistical advice, even when requests for which came at a moment's notice. How he put up with my bad moods, I'll never know. But, he did, and I'm grateful. Simone Kortstee and Peter Anderson provided unforgettable last-minute advice, ideas, and their precious time -- and I didn't even need to ask. Now that's friendship! I hope I can repay them someday. I'd also like to thank Jim Conway, Anna Fazekas, Steph Kennepohl, Suzanne Trudel, and, especially, Rita and John Smyth for opening their homes to me during my trips to Windsor. Without them I'd be even more in debt.

I couldn't end without thanking my parents, who have quietly allowed me to choose my own path in life. Such a gift cannot be repaid. Finally, to all the friends who have provided welcome words of support for the past two and a half years, thank you. I hope you will forgive me for not listing you all here. You know who you are.

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List of Abbreviations used in Tables

Subject groups

bi:	bilateral
BiT:	Bitemporal onset
CPG:	CPS with secondary generalization
CPS:	complex partial seizures
E:	persons with epilepsy
FL:	frontal lobe seizures
G:	generalized seizures
GM:	grand mal seizures
HS:	hippocampal sclerosis
LF:	left frontal onset
LT:	left temporal onset
NC:	normal controls
NCS:	no clinical seizures
NoHS:	no hippocampal sclerosis
P:	partial seizures
PC:	partial complex seizures
PE:	partial elementary seizure
PG:	primary generalized seizures
PM:	petit mal seizures
PsyM:	psychomotor seizures
RF:	right frontal onset
RT:	right temporal onset
TL:	temporal lobe seizures
UG:	undetermined generalized seizures
uni:	unilateral

Psychological tests and other variables

ACD:	Anticonvulsant drugs
AMIPB:	Attention and Memory Information Processing Battery
AVLT:	Auditory Verbal Learning Test
BDI:	Beck Depression Inventory

BNT:	Boston Naming Test
BVRT:	Benton Visual Retention Test
COWA:	Controlled Oral Word Association
CVLT:	California Verbal Learning Test
CVMT:	Continuous Visual Memory Test
del:	delayed recall
HAD:	Hospital Anxiety and Depression Scale
HRB:	Halstead-Reitan Neuropsychological Test Battery
imm:	immediate recall
LM:	Logical Memory subtest of the WMS
LMI:	Logical Memory subtest of the WMS-R, immediate recall
LMII:	Logical Memory subtest of the WMS-R, delayed recall
MAE:	Multilingual Aphasia Exam
MMPI:	Minnesota Multiphasic Personality Inventory
PAL:	Paired Associate Learning subtest of the WMS
PALI:	Paired Associate Learning subtest of the WMS-R, immediate recall
PALII:	Paired Associate Learning subtest of the WMS-R, delayed recall
POMS:	Profile of Mood States
QOLIE-89:	Quality of Life in Epilepsy - 89
RAVLT:	Rey Auditory Verbal Learning Test
RBMT:	Rivermead Behavioural Memory Test
ROCFT:	Rey-Osterreith Complex Figure Test
RPM:	Raven's Progressive Matrices
SRT:	Selective Reminding Test
TMT-B:	Trail Making Test - Part B
VDMT:	Verbal Memory Distractor Task
VR:	Visual Reproduction subtest of the WMS
VRI:	Visual Reproduction subtest of the WMS-R, immediate recall
VRII:	Visual Reproduction subtest of the WMS-R, delayed recall
WAIS-R:	Wechsler Adult Intelligence Scale - Revised
WAIS:	Wechsler Adult Intelligence Scale
WCST:	Wisconsin Card Sorting Test
WMS-R:	Wechsler Memory Scale - Revised
WMS:	Wechsler Memory Scale
WRMT:	Warrington Recognition Memory Test

CHAPTER I

INTRODUCTION

Factors Associated with Poor Memory Functioning in Persons with Epilepsy

Persons with epilepsy are often faced with difficulties related to their disorder that can affect their lives. These difficulties may include a number of psychological, social, and cognitive problems in addition to the clinical features of the disorder (i.e., seizures). The proposed study is particularly interested in the memory problems of which persons with epilepsy often complain. Indeed, a recent survey showed that approximately 50% of persons with epilepsy reported that memory problems presented a moderate or serious nuisance in their everyday lives (Corcoran & Thompson, 1993).

Neurobiological factors, such as duration of epilepsy and location of seizure onset, are typically presumed to have the greatest impact on memory functioning in persons with epilepsy and they have been the most common subject of research examining the correlates of memory problems in epilepsy. However, other cognitive and psychosocial factors also may influence memory performance. For example, in order to perform at an optimal level, perceptual, attentional, and response capabilities must be unimpaired. Similarly, psychosocial variables such as mood and motivation can influence performance on memory tests (Thompson, 1991). The influence of these factors on memory performance in persons with epilepsy has been relatively neglected in the literature. This is likely because epilepsy tends to be defined by its neurobiological factors and not by its cognitive and psychosocial factors. The purpose of this research is to examine the relationship between important neurobiological, cognitive, and psychosocial factors and memory performance in persons with epilepsy. Such an explicit multifactorial approach has not yet been employed to examine this topic.

The following case example is presented to illustrate that a number of factors that might influence memory test performance can be evident in a person with epilepsy.

> A 30-year-old single female with a high school education presented with a complaint of memory problems. She described having difficulty recalling conversations and remembering appointments. Laboratory results and seizure characteristics indicated a left temporal lobe seizure focus. There was a history of low achievement in school and mild depression. In her teenage years she was socially active, although she had difficulty initiating romantic relationships. She was unemployed and living with her parents. She was unable to drive and did not have easy access to public transport. Her anticonvulsant drugs caused her to feel "mentally slowed". Personality testing indicated mild depression and social introversion. A neuropsychological evaluation suggested the presence of a mild verbal learning deficit and poor verbal fluency in the context of normal general intellectual, visual-spatial, and attention / concentration skills.

There were many possible causes for this woman's mild verbal learning deficit. These included the left temporal lobe focus, mild depression, and generally inefficient verbal skills. Should it be concluded that her verbal learning deficit was primarily the result of the epileptogenic focus, or did the psychosocial and other cognitive factors also play a role? This issue is important for at least two reasons. First, if psychosocial factors were presumed to play a role in the clinical picture, intervention aimed at remedying these factors might serve to improve memory performance. In contrast, if the epileptogenic focus alone were presumed to underlie the verbal memory problem, treatment of psychosocial problems would seem a waste of resources with regard to the improvement of memory functioning. A better understanding of the factors associated with memory problems might help direct remediation efforts in a more efficient manner. Second, memory test results are used in presurgical assessments to evaluate the integrity of the left and right temporal lobes. A memory deficit, if found, provides part of the evidence for determining the site of seizure focus (Breier et al., 1996). If it were discovered that other

factors had a substantial influence on memory test outcome in individuals with temporal lobe epilepsy (TLE), then it would be important to consider these other factors before making conclusions about the site of seizure focus when a memory deficit is found. Thus, to investigate the variety of factors that may correlate with memory problems in persons with epilepsy, a multifactorial approach (advocated by Corcoran & Thompson, 1993, and Loiseau, Signoret, Strube, Broustet, & Dartigues, 1982), is employed in the present study.

Previous research that has investigated the relationship between various neurobiological, cognitive, and/or psychosocial variables and memory performance in epilepsy patients is reviewed in the next chapter. First, a description of epilepsy as a medical condition and a brief discussion of the concept of memory within clinical neuropsychology is presented to complete the introduction.

Epilepsy as a Medical Condition

The term seizure (also called ictus) refers to an "altered state of brain function" (DeLorenzo & Towne, 1989, p. 27) resulting from the abnormal synchronized discharges of groups of neurons. The manifestion of a seizure involves sensory, experiential, or motor phenomena, either in isolation or in combination. A seizure is a symptom of dysfunction in the gray matter of the brain rather than a disease in itself. The term epilepsy refers to a heterogeneous group of neurological disorders in which seizures occur repeatedly. As a clinical disorder, it is unique because it is defined by its clinical characteristics rather than its pathological substrates (Kapur, 1994).

Epidemiology

Epilepsy is among the most common neurological disorders in clinical medicine (Lothman & Collins, 1990). Incidence rates, or the number of new cases that occur

within a specified period of time, vary widely according to country and the criteria used to define epilepsy (Hauser, Annegers, & Anderson, 1983). However, average incidence rates range from 35 to 50 per 100,000 persons per year (Robertson, 1991; Thompson & Trimble, 1996). This translates to 60,000 to 150,000 new cases of epilepsy per year in the United States alone (DeLorenzo & Towne, 1989). The onset of epilepsy occurs in childhood or adolesence in approximately 60% of cases. In contrast, in less than two to three percent of cases is onset after the age of 50 years (DeLorenzo & Towne, 1989). Prevalence rates, or the number of cases that exist in a given population, also vary widely, although a prevalence rate of 5 per 1,000 persons appears to be the generally accepted standard (McIntosh, 1992a; Robertson, 1991). This translates to a minimum of 4 million individuals with some form of epilepsy in the United States (DeLorenzo & Towne, 1989).

Etiology

There are many possible causes of seizures (see Table 1). The more frequent causes of epilepsy are head trauma, infections and poisoning of the central nervous system, tumours, vascular disease, and chronic alcoholism (Thompson, 1991). Notably, among persons with TLE who present for surgical intervention, approximately 50% have medial temporal lobe sclerosis, or tissue hardening secondary to cellular degeneration (Falconer, 1971). These patients also tend to have seizure onset before the age of 10 years, a family history of epilepsy, and a history of febrile convulsions in infancy.

Insert Table 1 about here

Seizure etiology may play a significant role in the presence of cognitive and/or memory deficits. For example, idiopathic epilepsy, or epilepsy with no identifiable cause and often a hereditary component, is not usually associated with cognitive deficits

(Dreifuss, 1992). In contrast, acquired or symptomatic epilepsy is often accompanied by cognitive deficits and other neurological signs, depending on the location and extent of brain dysfunction.

Epileptogenesis

Epileptogenic neurons typically produce unpredictable, sudden, excessive discharges, called paroxysms. A paroxysmal event can occur as an isolated incident between seizures or as a precursor to a seizure (Lothman & Collins, 1990). Interictal (between seizures or icti) paroxysms produce a characteristic spike-and-wave formation on an electroencephalograph (EEG). The location of the interictal spike-and-wave discharges measured by EEG is used to estimate the location of seizure focus in focal epilepsy. However, interictal paroxysms located far from the surface of the brain cannot be detected by EEG.

When a paroxysm develops into a seizure the abnormal discharge spreads to assemblies of cells which, in turn, discharge abnormally, producing various behavioural manifestations such as jerking movements, stereotyped movements, sensory experiences, loss of awareness, convulsions, and loss of consciousness. The particular clinical manifestation of the seizure depends on the site of the focus in the cortex and on the location and extent of connected sites (Adams & Victor, 1993).

Classification of seizures

Seizures are classified according to their clinical features (see Table 2). For the purpose of classification, seizures can be defined as partial (focal) or generalized. Partial seizures are further differentiated into simple (no alteration of awareness) or complex (alteration or loss of awareness; Commission on Classification and Terminology of the International League Against Epilepsy, 1981). A partial seizure involves a relatively

circumscribed region of the brain. In contrast, a generalized seizure involves widespread connections throughout the brain. Generalized seizures all involve loss of awareness and are commonly differentiated into two types: generalized tonic-clonic (previously called grand mal) and absence (previously called petit mal). Finally, a partial seizure which begins at a particular focus can spread bilaterally throughout the brain and thus become secondarily generalized.

Insert Table 2 about here

Partial seizures

Two-thirds of adults with epilepsy and almost half of children with epilepsy have partial epilepsies (Adams & Victor, 1993). Simple partial seizures arise from a discrete cortical focus, most often in the sensorimotor cortex. By definition they do not involve alteration of consciousness. Simple partial seizures are often referred to as auras when they precede complex partial or generalized seizures. An aura should be differentiated from a prodrome which refers to the perception that a seizure will occur in the near future. A prodrome could be a change in mood, myoclonic jerk, headache, or autonomic symptom (Adams & Victor, 1993).

Simple partial seizures with motor signs often arise from a focus in the frontal lobe contralateral to the affected side of the body (Adams & Victor, 1993). The most common features are turning movements of the head and eyes to the contralateral side, often accompanied by tonic contractions of the trunk and limbs. Simple partial seizures with somatosensory signs usually arise in or near the postrolandic convolution of the contralateral cerebral hemisphere. Clinical characteristics include numbness, tingling, and/or other tactile sensations. Seizures involving elemental visual sensations such as

colour and light localize to the occipital lobe. Visual hallucinations, on the other hand, are more commonly associated with a focus in the posterior part of the temporal lobe. They may be associated with auditory hallucinations, although the latter are infrequent (Adams & Victor, 1993). Partial seizures involving other psychic phenomena such as feelings of unreality, deja vu, feelings of depersonalization, fear, anger, delusions, sexual feelings, and paranoia are also commonly related to a seizure focus in the temporal lobe or limbic system (Kandel, 1991). Other reported manifestations of simple partial seizures include vertiginous sensations, visceral sensations, olfactory hallucinations, and gustatory hallucinations.

Complex partial seizures also arise from a discrete cortical focus, most often in the temporal lobe, but the clinical features include alteration of consciousness (Adams & Victor, 1993). Often, an aura occurs in the first phase. Subsequently, there is a period of altered behaviour and consciousness that the individual does not later recall. Motor activity can occur in the form of an automatism (i.e., a stereotyped, involuntary motor activity; Lothman & Collins, 1990). Common automatisms involve lip-smacking, chewing or swallowing movements, fumbling of hands, picking at clothes, or shuffling of feet. The patient may also walk or speak in an incoherent fashion. Other terms occasionally used to refer to a complex partial seizure are psychomotor seizure, temporal lobe seizure, or limbic system seizure. Of persons with epilepsy who are over 30 years of age, approximately 55% to 65% have TLE (Stevens, Millstein, & Goldstein, 1972). Following a complex partial seizure, a period of postictal confusion is common.

Generalized seizures

Generalized seizures are not typically associated with a particular focus and can arise bilaterally and symmetrically. The classic generalized tonic-clonic seizure begins with a 10 to 20 second tonic phase during which the person falls and the musculature is

seized in a tonic spasm. It is followed by a clonic phase during which there is a repetitive relaxation of the tonic contraction (beginning at a rate of 8 per second and progressing to a rate of 4 per second) followed by brief, violent, rhythmic, flexor spasms that gradually decrease in amplitude and frequency during the last 30 seconds of the seizure (Adams & Victor, 1993). A coma-like state lasting 5 minutes commonly ensues. Upon wakening the individual is often initially confused. There is no recollection of the seizure, although if there had been an aura it might be recalled. A prolonged series of generalized tonic-clonic seizures, called status epilepticus, is a dangerous condition requiring urgent treatment as serious physical injury can occur and normal respiration ceases.

The hallmark of an absence seizure is temporary interruption of consciousness. Postural tone usually remains relatively intact (i.e., the person does not fall). In most cases there are also brief and subtle movements, and automatisms such as lip smacking, chewing, and fumbling may occur. There is no postictal period of confusion. Rather, the person returns to full consciousness after the seizure. Atypical absence seizures involve less complete loss of consciousness or more promient myoclonus. Approximately 30 percent of children with absence seizures also display symmetrical or asymmetrical myoclonic jerks without loss of consciousness, and about 50 percent will experience generalized tonic-clonic seizures at some time (Adams & Victor, 1993).

Classification of epilepsies and epileptic syndromes

Type of epilepsy is typically classified according to the seizure types outlined in Table 2. This method of classification is used at present because no other diagnostic procedure is currently available that would substantially improve classification (Kapur, 1994). Nevertheless, a second classification system has been devised to delineate epilepsies and epileptic syndromes (see Table 3). Some of these epileptic disorders represent diseases with a common etiology and prognosis, whereas others are syndromes

for which a common etiology may be found in future (Commission on Classification and Terminology of the International League Against Epilepsy, 1989). They are presented in Table 3 according to whether they are partial or generalized in origin.

Insert Table 3 about here

Anticonvulsant drugs

A wide variety of anticonvulsant drugs are available for treatment of seizures. The type of anticonvulsant is usually chosen according to the type of seizure to be treated and the risk of side-effects. The most common anticonvulsants, and the types of seizures for which they are prescribed, are listed in Table 4. In general, treatment with one anticonvulsant is preferred to polytherapy, both in terms of improved seizure control and risk of side-effects (McIntosh, 1992b). In addition, the risk of cognitive impairment due to anticonvulsant drug effects appears to be reduced with monotherapy (Thompson, 1992).

Insert Table 4 about here

Memory as a Neuropsychological Concept

When a patient complains of a "memory problem" it is necessary to enquire further in order to determine the precise difficulty. This is because a number of processes are involved in encoding, storing, and retrieving new memories. In order to uncover the nature of a memory problem, first, it must be established that initial sensory systems (e.g., vision and audition) are functioning adequately so that the patient can perceive the

incoming information properly. Second, there must be enough attentional capacity to allow for registration and encoding of the new information. Third, a process by which this newly encountered information is stored must operate. Fourth, there must be a process by which stored information can be retrieved at a later stage. This theoretical conceptualization of memory functioning is remarkably simplified and does not consider the influence of situational factors. However, it is presented here as a background to a discussion of the types of memory tests used by clinical neuropsychologists.

The studies described in the next chapter utilize various memory tests that purport to measure selected aspects of memory. It is notable, however, that the storage and retrieval stages of memory are usually of primary interest in the assessment of memory functioning. Thus, most memory tests involve at least two phases. In the study phase new information is presented to the individual and he or she attempts to store this new information. In the test phase the individual is asked to retrieve the previously presented information. Retrieval can be assessed using a free recall, cued recall, or recognition memory format. The various aspects of memory can be measured in both the verbal and visual-spatial domains.

Four types of memory tests are typically used to assess different aspects of the storage and retrieval of verbal or visual-spatial information. First, immediate recall tests measure the amount of new information that can be retrieved immediately after presentation. The to-be-remembered-information is designed to exceed the individual's immediate memory span such that optimal performance depends upon storage and retrieval processes operating over the very short term. For example, during the Logical Memory I subtest of the Wechsler Memory Scale - Revised (WMS-R; Wechsler, 1987), the examiner reads a short story to the participant, and the participant is instructed to recall as much information from the story as possible immediately afterward. Second,

delayed recall tests measure the amount of new information that can be retrieved after a delay; usually a delay of 20 minutes to 1 hour. It involves both storage and retrieval mechanisms, but also taps the individual's ability to retain information. For example, during the Logical Memory II subtest of the WMS-R, the participant is instructed to recall two short stories 30 minutes after presentation. Third, performance on a learning test requires ability to store and retrieve new information, as well as ability to benefit from repetition of the to-be-remembered information. An example of a test in this domain is a word list learning test during which a list of words is read to the participant on five successive trials, and the participant is instructed to recall as many words as possible after each presentation of the list. Learning is represented by the increment in number of words recalled from the first to the fifth trial. Fourth, recognition memory tests measure the participant's ability to discriminate between previously presented test material and new material. At the test phase, the individual is instructed to choose the items that were presented in the study phase, and reject the items that were not previously presented. If an individual is able to recognize significantly more items in this format than he or she could recall, it is speculated that a deficiency in the storage, retention, and/or retrieval process is manifested as retrieval inefficiency.

The types of memory measures outlined above -- immediate recall, delayed recall, learning, and recognition memory -- are used in both the verbal and visual-spatial domains. The distinction between verbal and visual-spatial memory depends on the type of information presented. During a verbal memory test, information is typically presented in a written or spoken format; during a visual-spatial memory test, information is typically presented in a visual format as drawings or pictures. However, there may be overlap in the way these types of information are processed by an individual. For example, one who prefers to process information verbally may translate visual-spatial

information into a verbal representation. Conversely, it is possible to visualize verbal information such as a word list. Indeed, this is a good strategy to use to aid recall.

* * * * *

In this introductory chapter, the rationale for this study was described and information about epilepsy and the measurement of memory was presented. In the next chapter, a review of the literature pertaining to memory functioning in persons with epilepsy is presented. In addition, conclusions regarding the factors that are most consistently associated with poor memory functioning in persons with epilepsy are made.

CHAPTER II

LITERATURE REVIEW

Factors Associated with Poor Memory Functioning in Persons with Epilepsy: A Review of the Literature

The relationship between epilepsy and cognitive problems in general, and memory problems in particular, has received significant attention only since the late 19th century (Bennett, 1992; Haynes & Bennett, 1992). Until that time, the prevailing opinion was that cognitive and mental deterioration, as well as personality disturbance, were invariably linked with epilepsy. The latter half of the 19th century saw an awakening of a more scientific approach to medicine and, in 1861, Russell Reynolds challenged the prevailing opinion. Buchwald and Devinsky (1988), in their review of the contribution of Reynolds to the study of interictal symptoms in epilepsy, noted that "The conclusion that severe mental illness was present in almost all persons with epilepsy was recognized by Reynolds as an artifact of patient selection and failure to exclude cases with concomitant medical illness or structural brain lesions" (p. 803). Reynolds used his own observations of patients, as well as observations made by patients' family members and friends, to evaluate the mental status of 62 community dwelling patients with idiopathic epilepsy. He found that 39% of the patients he evaluated possessed "normal" mental status. Thirty-two percent of the patients displayed mild "recent memory" impairment, and only 14.5% of the patients displayed moderate or severe cognitive impairment (Buchwald & Devinsky, 1988). Thus, his results contradicted the notion that mental deterioration was necessarily associated with epilepsy.

While Reynolds' contribution to the study of cognitive problems in persons with epilepsy was an important turning point, it was not until the 1950s that more

representative estimates of the prevalence of cognitive impairments emerged. In 1960, Lennox and Lennox published the book Epilepsy and related disorders in which they studied over 1,000 patients and concluded that two-thirds were intellectually normal and only one in seven persons with epilepsy showed an unequivocal cognitive impairment (Thompson & Trimble, 1996). Furthermore, among patients seen in private practice, one quarter had IQs greater than 120. Current estimates of the number of persons with epilepsy with substantial cognitive deterioration range from 10 to 20% (Dodrill, 1988).

The memory test scores of groups of persons with epilepsy are consistently poorer than normal control groups (e.g., Loiseau, Strube, Broustet, Battellochi, Gomeni, & Morselli, 1983; Randolph, Gold, Kozora, Cullum, Hermann, & Wyler, 1994). Thus, it is not surprising that many previous research endeavours have attempted to elucidate the variables that are associated with memory impairment. Neurobiological factors have been the most common subject of research in this area. Still, cognitive and psychosocial factors also may be related to memory performance in persons with epilepsy (Christianson, 1994). The tendency to ignore other cognitive and psychosocial sources of variance likely reflects the way that memory traditionally has been assessed as a distinct "entity" while virtually ignoring the "flexibility of the human cognitive system" (Nilsson, Christianson, Silfvenius, & Blom, 1984, p. 44). In the present study, a relatively broad view of the factors that may be associated with memory impairment in persons with epilepsy is taken.

A multietiological approach

Since the 1950s, a number of advances have improved the study of memory in persons with epilepsy. For instance, psychological testing has become increasingly refined, and the multiple factors that can influence performance on cognitive tests have become better appreciated. Technical advances have improved the ability to locate

epileptiform activity and assess cerebral pathology. Attention to the psychosocial factors associated with epilepsy, as well as the cognitive correlates, has increased (Haynes & Bennett, 1992). Also, a larger variety of anticonvulsant drugs has been developed. Consequently, by the late 1980s a wide variety of factors that could be associated with memory problems in persons with epilepsy had been examined. However, no one factor emerged that could account for the majority of variance in memory test performance – although location of seizure focus appeared to play a role. Rather, the relatively low memory performance often displayed by persons with epilepsy, as a group, appeared to be related to multiple factors. Hence, a multietiological approach to evaluating memory performance in persons with epilepsy has been advocated (Corcoran & Thompson, 1993; Loiseau, Strube, & Signoret, 1988). Such an approach would examine neurobiological, cognitive, and psychosocial factors that could be associated with memory performance. By "(i) taking into account the factors which may operate often in combination; and (ii) using very sensitive measures of memory" it may be possible to identify subgroups of persons with epilepsy who are particularly sensitive to specific types of memory problems (Loiseau et al., 1988, p. 173).

Despite the recommendation of a multietiological approach, most research has remained focused on neurobiological factors (e.g., Dreifuss, 1992). A multietiological approach would be greater in scope and might require more resources than a more restricted study. Nevertheless, it is warranted. "An important goal in taking a more scientific approach to epilepsy is to attempt to characterize this multifaceted condition, to be able to separate out groups that have similar traits and possibly similar etiologies" (DeLorenzo & Towne, 1989, p. 28).

In the review to follow, first, neurobiological factors are reviewed. These include seizure-related variables, location of seizure onset, hippocampal pathology, cerebral

pathology, and anticonvulsant drugs. Second, cognitive factors other than memory functioning are reviewed. Finally, psychosocial factors are reviewed. The collective findings of the review are used to formulate the hypotheses for the present study.

Neurobiological Factors

The relationship between seizure-related variables and memory performance

Initial inquiries into the correlates of memory deficits in persons with epilepsy examined seizure-related variables (see Table 5). This would seem a logical place to begin, as seizure-related factors are specific to persons with epilepsy. These variables included age at seizure onset, duration of epilepsy, seizure frequency, seizure type, and etiology.

Insert Table 5 about here

Seizure frequency

Given the possible link between repeated seizures and the cerebral pathology often seen in epileptic brains (e.g., hippocampal sclerosis; Norman, Sandry, & Corsellis, 1974), and the link between cerebral pathology and cognitive functioning, it is reasonable to consider the possible detrimental effect of high seizure frequency on memory functioning. However, there is little objective evidence to suggest that seizure frequency is associated with memory functioning. A number of studies have failed to find a significant correlation between seizure frequency and memory performance (Brittain, 1980; Delaney, Rosen, Mattson, & Novelly, 1980; Rausch, Lieb, & Crandall, 1978). Other studies that subdivided patients into groups according to seizure frequency either failed to find a significant effect (Loiseau et al., 1980; Scott, Moffett, Mathews, &

Ettlinger, 1967) or found inconsistent results (Loiseau et al., 1982; 1983). Also, one study found that seizure frequency did not provide a unique contribution to the variance in total memory score according to multiple regression analysis (Loiseau et al., 1982). Finally, Dodrill (1986) examined a variable that is related to both generalized seizure frequency and duration of illness: lifetime number of seizures. Dodrill divided patients into groups ranging from a total of two to 10 generalized tonic-clonic seizures, to more than 100 generalized tonic-clonic seizures. He found no effect of lifetime number of seizures on immediate recall of short stories or figures.

Seizure type

Many studies have investigated the effect of different seizure types on memory performance. In particular, because psychomotor or complex partial seizures have been associated with the temporal lobes, and the temporal lobes have been associated with memory storage and retrieval, the association between complex partial seizures and memory functioning has been scrutinized. In addition, the effect of status epilepticus or severe tonic-clonic seizures have been a topic of enquiry.

Overall, studies evaluating the relationship between seizure type and memory have yielded mixed results. Hermann , Wyler, Steenman, and Richey (1988) found no correlation between having more than one seizure type and verbal learning performance in persons with left TLE. Furthermore, Loiseau et al. (1982) found that seizure type did not provide a significant unique contribution to the variance in total memory score according to multiple regression analysis, and patients with generalized, simple partial, and complex partial seizures all had poorer verbal and visual memory scores in comparison with normal controls. In addition, another study by Loiseau and colleagues (1980) found no effect of epilepsy type on memory, and Homan et al. (1989) found no

differences among patients with simple partial, complex partial, secondarily generalized, or mixed seizure types on memory performance.

In contrast, other studies have found that seizure type can be related to performance on particular memory tasks. Schwartz and Dennerll (1969) found that occurrence of psychomotor seizures was associated with poor immediate reproduction of figures whereas occurrence of grand mal seizures was less important. In addition, Bornstein, Pakalnis, Drake, and Suga (1988) found that patients with complex partial seizures performed relatively poorly on various visual-spatial memory tasks, whereas presence of generalized seizures was not related to memory performance in any consistent or remarkable way. The results suggested that the presence of complex partial seizures was related to memory performance in the visual-spatial domain, but not in the verbal domain. However, these results might well be due to a preponderance of patients with right sided seizure foci in their sample. Taken together, these studies suggest that psychomotor or complex partial seizures can have a detrimental effect on memory, whereas grand mal or generalized seizures are less important.

Contrary to the above, Loiseau et al. (1983) found that patients in each of four seizure groups (see Table 5), obtained poorer mean verbal learning scores than corresponding control groups, whereas only the primary generalized seizure group displayed poorer visual-spatial recall scores than controls. Another study by Loiseau and colleagues (1982) found that, when considering the percentage of information retained after a delay, only the generalized seizure group was poorer than controls. (As noted above, when considering raw test scores in this study, all seizure groups displayed poorer memory performance than controls). A subsequent study by Loiseau, Signoret, and Strube (1984) found that patients with generalized seizures obtained poorer learning and

memory scores than matched controls, whereas patients with partial seizures obtained learning and memory scores that were equivalent to matched controls.

Finally, status epilepticus may have particular effects on cognitive functioning because it can be associated with more severe symptoms such as anoxia during prolonged episodes (Adams & Victor, 1993). Dodrill (1986) found that patients with a history of status epilepticus obtained poorer immediate figural recall scores than patients with a lifetime history of 11 to 100 tonic-clonic seizures. History of status epilepticus was not significantly related to performance on immediate story recall. However, patients with status epilepticus also obtained significantly poorer IQ and neuropsychological impairment scores and were at greater risk for general cognitive impairment.

Etiology

The sparse studies regarding the effect of seizure etiology on memory functioning have yielded little in the way of conclusive findings. Hermann et al. (1988) found no correlation between etiology (idiopathic, symptomatic or unknown) and measures of verbal learning. Similarly, Homan et al. (1989) found no difference between patients with epilepsy secondary to head trauma and patients with epilepsy of undetermined origin on memory. On the other hand, Brittain (1980) found that the performance of patients with unknown etiology was superior to patients with known etiology on measures of recognition memory.

The lack of research in this area is likely due to the fact that one category of seizure etiology may produce a variety of outcomes in terms of cerebral pathology. For example, a brain aneurysm could occur in the anterior communicating artery, the posterior cerebral artery, or any one of a number of other locations. Moreover, a brain tumour in the same location could range in diameter from 10 mm to 10 cm. Thus, it is more logical to consider the effect of demonstrable cerebral pathology in relation to

etiology, rather than simply the effect of a particular etiology. The relationship between demonstrable cerebral pathology and memory performance is discussed in a later section.

Age at seizure onset

The hypothesis that the age at which a person's epilepsy began influences the development and severity of a memory deficit has been evaluated by a number of researchers. In particular, many have speculated that earlier age at seizure onset is related to poorer memory outcome. It should be borne in mind that any investigation of the unique influence of age at onset may be complicated by the interrelationship between age at onset and duration of epilepsy. For the moment this issue will be put aside in order to consider the research that has investigated the influence of age at seizure onset on memory performance.

Most studies that have examined the correlation between age at seizure onset and memory have failed to find a significant relationship (Delaney et al., 1980; Hermann et al., 1988; Scott et al., 1967; Seidenberg, Hermann, Haltiner, & Wyler, 1993). Loiseau and colleagues (1982) found that age at onset did not provide a significant unique contribution to the variance in memory score according to multiple regression analysis. In addition, they subdivided patients into three groups according to age at onset. All groups had poorer raw memory scores when compared to normal controls. However, when considering the percentage of information retained after a delay, only the adolescent onset group was poorer than controls. In a later study using different memory tests, Loiseau and colleagues (1983) found that the early onset group (i.e., before 10 years of age), performed more poorly than controls on word list learning, the adolescent onset group (i.e., between 10 and 17 years of age), was relatively deficient on word list learning and immediate recall of figures, and the later onset group (i.e., after 17 years of age), was relatively poor on word list recognition. The results of Loiseau et al. (1983) did not

produce a consistent pattern related to age at seizure onset and memory performance, although patients with onset during adolescence may have been more impaired overall, with memory deficits in both the verbal and visual-spatial modalities. Taken together, the two studies by Loiseau et al. (1982, 1983) suggested that adolescent onset of seizures had a detrimental effect on memory performance, whereas onset before or after adolescence may have little independent effect on memory performance. As these studies did not compare the patient groups to each other, it is not known whether patients with adolescent onset performed more poorly than patients with onset at other ages.

Two other studies found contrasting results. Baxendale et al. (1998) found that later age at onset predicted poorer delayed story recall and immediate figure recall, whereas Saykin, Gur, Sussman, O'Connor, and Gur (1989) found that TLE patients with seizure onset at or before five years of age displayed poorer overall memory performance than patients with seizure onset after five years of age.

Strauss, Wada, and Hunter (1992) examined the differential effect of very early onset (i.e., before one year of age) on male versus female persons with epilepsy. Their results indicated that male patients, regardless of lateralization of speech dominance, and female patients with atypical speech dominance (i.e., speech dominance in the right hemisphere or both hemispheres), obtained poor memory scores. Female patients with left hemisphere speech dominance showed average memory performance. Their analyses employed quite small group sizes, but the results suggested that very early seizure onset could have a negative effect on memory, and this effect was mediated by the gender of the patient and the development of typical speech dominance.

Duration of epilepsy

A number of the studies that examined the correlation between duration of epilepsy and memory failed to find a significant relationship (Hermann et al., 1988;

Rausch et al., 1978; Scott et al., 1967). In addition, Loiseau and colleagues (1980) divided 100 persons with epilepsy with "normal social adjustment" into four groups ranging from a duration of less than 1 year to a duration of more than 10 years, and found no effect of duration on immediate figural recall, word list learning, or recognition memory.[1] In a later study, Loiseau and colleagues (1983), against expectation, found that patients with a duration of epilepsy of less than 21 years obtained poorer word list learning scores than normal controls, whereas patients with a duration of greater than 20 years showed no significant difference from normal controls. Thus, they found that both shorter duration and early onset (see previous section) were associated with relatively poor word list learning scores. They made no attempt to reconcile these apparently discrepant results.

In contrast, other researchers found that longer duration of epilepsy was significantly correlated with poor memory performance (Delaney et al., 1980; Mirsky, Primac, Marsan, Rosvold, & Stevens, 1960). Also, Baxendale et al. (1998) found that duration (along with age and right hippocampal volume) contributed to prediction of delayed figure recall in TLE patients. Loiseau et al. (1982) found that, when considering the percentage of information retained after a delay, only patient groups with longer duration (i.e., more than 12 years) performed more poorly than controls. However, with regard to raw memory scores, patients performed more poorly than normal controls regardless of duration of illness. In this study using patients with relatively "normal social adjustment", duration of epilepsy did not provide a significant unique contribution to the variance in total memory score.

Loiseau et al. (1982) also investigated the way duration interacted with other epilepsy related factors in relation to memory test performance. They grouped patients

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[1] They did not present statistical results to support this finding and described the research as "in progress".

according to duration of epilepsy (i.e., less than 12 years vs. more than 12 years) and then further subdivided patients according to age at seizure onset (i.e., early vs. adolescent vs. late), seizure frequency (i.e., less than one seizure per month vs. more than one seizure per month), or seizure type (i.e., generalized versus partial seizures). In all cases, patient groups obtained total memory scores that were lower than normal controls, with one exception. Normal memory performance was seen in patients with a relatively short duration of epilepsy and an absence of partial seizures.

Only one study has specifically investigated the effect of duration on verbal and visual-spatial memory in left temporal lobe (LTL) versus right temporal lobe (RTL) patient groups (Làdavas, Umiltà, & Provinciali, 1979). Patients who had a duration of epilepsy of greater than one year obtained a greater discrepancy between their verbal and visual-spatial learning and delayed recall scores than those having a duration of less than one year. These findings suggested that longer duration was associated with a greater relative decrement in verbal memory in LTL patients and a greater relative decrement in visual-spatial memory in RTL patients.

Summary

The first approach used to examine the correlates of memory functioning in persons with epilepsy investigated seizure-related variables such as seizure frequency, seizure type, etiology, age at seizure onset, and duration of epilepsy. The methodological difficulties inherent in these studies have made it difficult to isolate the impact of a single factor. For example, age at onset and duration of epilepsy are obviously interrelated but they could have independent effects on memory functioning. Even so, the results of these investigations have been relatively disappointing. It appears that much of the variance in memory functioning among persons with epilepsy is not specifically due to these seizure-related variables.

The relationship between seizure type and memory performance remains equivocal. Some studies found no effect (Hermann et al., 1988; Homan et al., 1989; Loiseau et al., 1980), others found that complex partial seizures were related to memory deficits (Bornstein et al., 1988; Schwartz & Dennerll, 1969), whereas others found that both generalized and partial seizures were related to memory deficits (Loiseau et al., 1982; 1983; 1984). It should be noted that the Bornstein et al. (1988) and Schwartz & Dennerll (1969) studies compared patient groups defined by patient type to each other, whereas the Loiseau et al. studies compared partial and generalized seizure groups to their respective control groups. This difference in methods of comparison might have underlain the discrepant findings. Changes in research trends have meant that, increasingly, patients are classified according to location of seizure onset rather than seizure type.

Case studies may indicate that persons with seizures secondary to brain damage display greater memory problems than patients with no demonstrable brain damage, but empirical evidence based on group studies is mixed (Brittain, 1980; Hermann et al., 1988; Homan et al., 1989). Most studies have not found a significant relationship between age at onset and memory (Delaney et al., 1980; Hermann et al., 1988; Scott et al., 1967; Seidenberg et al., 1993; Loiseau et al., 1982, 1983). One study found that onset before six years of age was detrimental to memory performance (Saykin et al., 1989) whereas another found that later age at onset predicted poor memory performance (Baxendale et al., 1998).

The seizure-related factor that appears to have the most consistent detrimental effect on memory performance is longer duration of epilepsy (Baxendale et al., 1998; Delaney et al., 1980; Làdavas et al., 1979; Loiseau et al., 1982; Mirsky et al., 1960), although some studies have not found a significant relationship (Hermann et al., 1988;

Loiseau et al., 1980, 1983; Rausch et al., 1978; Scott et al., 1967). The effect of duration may reflect the cumulative effect of repeated seizures, the long term use of anticonvulsant drugs, or a combination of both. However, evidence for a significant relationship between seizure frequency and memory performance has not been found (Brittain, 1980; Delaney et al., 1980; Dodrill, 1986; Loiseau et al., 1980; Rausch et al., 1978; Scott et al., 1967).

During the past 20 years, research emphasis has shifted from examining the role of the seizure-related variables described above to examining the role of the location of seizure focus or cerebral pathology in more detail. In the next section, research that has investigated the ways in which location of seizure focus may be related to memory deficits is examined.

The relationship between location of seizure focus and memory performance

The relationship between the side of temporal lobe epileptogenic focus and material-specific memory impairment became an important research issue in the wake of results indicating material-specific memory deficits in post-surgical epilepsy patients with unilateral temporal lobe lesions (Milner, 1971). Patients with LTL lesions displayed relatively poor verbal memory whereas patients with RTL lesions displayed relatively poor visual-spatial memory. In addition, recent advances in technology and resources have allowed researchers to localize seizure focus and cerebral pathology with a greater degree of accuracy. Hence, many studies have attempted to relate the location of the seizure focus to specific memory deficits in an effort to understand the memory problems common in persons with epilepsy who have not undergone surgical removal of the epileptogenic focus.

The techniques used to define the location of seizure focus have ranged from clinical judgement and scalp EEG (see Table 6) to comprehensive presurgical

investigations using multiple laboratory tests (see Table 7). The location of abnormal spike-and-wave activity recorded by scalp EEG electrodes is often used to infer the location of an epileptogenic focus. However, an interictal EEG may fail to record electrical abnormalities that are far from the surface of the brain, and a twenty minute EEG may fail to record paroxysmal activity that occurs at other times during the day. Hence, the present methodological standard employs, at least, 24 hour video EEG in order to capture the characteristics of electrical activity in the brain during a seizure. When this technique does not provide satisfactory results, subdural electrode strips may be inserted to record electrical activity more precisely. Even when seizure focus is determined for surgical intervention using the most advanced techniques, contralateral brain abnormalities may exist in persons with TLE, rendering patient groups somewhat heterogeneous (Incisa della Rocchetta et al., 1995). Therefore, discrepancies among studies in this area might not be unexpected.

A shift toward using only epilepsy surgery candidates in research of this type began in the late 1980s (see Table 7). This shift was largely due to the expansion of epilepsy surgery programmes around the world. In this section, studies that have compared different subgroups of persons with epilepsy, defined according to location of seizure focus, are reviewed. First, studies that employed patients who were not epilepsy surgery candidates are reviewed. This is followed by a review of studies employing epilepsy surgery candidates.

Insert Table 6 about here

Non-surgical candidates

As early as 1960, Mirsky and colleagues attempted to relate seizure type and seizure focus to memory performance. They found that differences in WMS Memory Quotient (MQ) performance were not attributable to the location of seizure focus, although side of seizure focus was not specifically examined. In 1973, Glowinski found that persons with TLE had lower immediate story recall and IQ-MQ discrepancy scores than a group with generalized epilepsy. Notably, there were reported IQ differences between the two groups, although the exact nature of these differences was not described. Glowinski concluded that the differences in story recall were not due to differences in IQ because of the results for IQ-MQ discrepancy. However, this is not a valid method of controlling the influence of IQ on memory (Larrabee, 1987; Lezak, 1995; Prigatano, 1978) and there were no procedures to ensure that the difference between groups for immediate story recall was independent of IQ. Finally, Glowinski stated that "There was no significant relationship between laterality of the temporal lobe epileptogenic lesion and impairment of verbal and nonverbal memory task performance on the WMS. Although ... the differences that do exist are, once again, in the predicted direction" (p. 133). This result has often been cited as not supporting the hypothesis that unilateral TLE is associated with material-specific memory deficits. However, there was no specific reference to how laterality was determined, to a statistical analysis, or to the number of temporal lobe patients assessed in the analysis.

Rausch and colleagues (1978) examined the degree of lateralized depth spike activity in persons with epilepsy and its relationship with memory performance. The degree of lateralized activity was positively correlated with WMS MQ score. Also, having a majority of spike activity in the right temporal area was positively correlated with measures of verbal memory. It is important to note that these were preliminary

findings and only 4 of the 12 patients had a majority of spike activity in the left temporal area.

Other studies have examined the effect of side of seizure onset more specifically. Mungas, Ehlers, Walton, and McCutchen (1985) compared patients with RTL versus LTL seizure onset on verbal learning and recall and failed to find significant differences between the groups. However, they found that the LTL patients had poorer phonemic cued recall and lower delayed recall scores relative to their learning score. The duration of the delay period was not reported and it is possible that the recall trial occured after one intervening distractor trial without any additional period of delay. If this were the case, the learning minus delayed recall score might represent a retroactive interference (RI) effect rather than a delayed recall or forgetting effect. Finally, there was no control for naming or language-related problems that might account for the LTL deficits. Mayeux, Brandt, Rosen, and Benson (1980) explicitly examined the relationship between language deficits and memory in persons with LTL and RTL epilepsy and individuals with generalized seizures. It should be noted that the patients in this study were "volunteers" from specialist epilepsy clinics and it was not clear whether the patients were self-selected participants. They found no significant intergroup differences on any of the memory tests (see Table 6). However, they did find that the LTL group performed significantly more poorly on a picture naming test. These authors concluded that patients with a LTL focus do not have a particular memory impairment but, rather, they have a naming impairment that masks itself as a memory problem. Of course, this hypothesis does not account for persons with epilepsy who have a memory problem but do not have a LTL focus or a naming problem. Nonetheless, this study made a contribution by emphasizing the importance of accounting for other possible underlying cognitive deficits such as naming or concentration before concluding that any performance decrement is

due to memory per se. This issue will be addressed in greater detail in the later section on the relationship between other cognitive functions and memory performance.

Loiseau et al. (1983) evaluated a group of persons with epilepsy who were working or attending school and maintained relatively "normal social adaptation". Patients were assigned to one of four groups according to location of seizure focus in the left or right temporal or left or right frontal region. They found no significant differences between each of these patient groups and their respective control groups on three memory measures. In contrast, they found that a group of 91 patients with bilateral epileptiform activity obtained poorer immediate figural recall and word list learning scores in comparison to normal controls. Another study by Loiseau et al. (1982), found both verbal and visual memory deficits in patients with a unilateral EEG focus (in either the frontal or temporal lobe) when compared to control groups. Patients with bilateral EEG foci showed the same deficits, but, in addition, they showed deficits in percent retained after a delay.

Andrewes, Puce, and Bladin (1990) attempted to predict side of temporal lobe seizure focus by comparing interictal memory performance to postictal memory performance. A decline in verbal recognition memory score from the interictal to the postictal period was associated with a left temporal focus and a decline in figural recognition memory from the interictal to the postictal period was associated with a right temporal focus. This study suggested that a material-specific decline in recognition memory performance corresponded to unilateral EEG slowing in the postictal phase. It should be noted that their sample size was small and there were no intergroup differences in memory performance during the interictal phase.

The studies described so far have not provided compelling evidence to support the notion that unilateral temporal lobe seizure focus is associated with material-specific

interictal memory performance. However, other researchers have found significant material-specific memory deficits according to seizure focus location. Giovagnoli & Avanzini (1996) found that verbal long term retrieval was poorer in patients with a LTL seizure focus (determined via ictal EEG), relative to both a RTL group and a normal control group. Similarly, Tröster and colleagues (1989) found that LTL patients were relatively deficient on a number of verbal memory measures when compared to RTL patients and normal controls.

Visually presented information can be presented independently to each cerebral hemisphere using a visual half-field technique.[2] Masui et al. (1984) employed this technique in order to assess the role of each temporal lobe in verbal recognition memory. Patients with a LTL focus displayed poorer retention of words presented to the left hemisphere but there was no effect for RTL focus patients. Nonverbal (i.e., pictorial) stimuli were not used in this study because pilot research indicated overly poor performance in that modality.

Other studies have found material-specific memory deficits in persons with TLE using both verbal and visual-spatial tests. Làdavas et al. (1979) found that RTL and LTL groups obtained different long term memory difference scores (i.e., verbal minus visual-spatial memory scores) but there was no difference between right and left frontal lobe groups. The right temporal group obtained positive difference scores (i.e., relatively poor visual-spatial memory performances) and the left temporal group obtained negative difference scores (i.e., relatively poor verbal memory performances). In addition, within the right hemisphere, the temporal group obtained positive difference scores and the frontal group obtained negative difference scores. Within the left hemisphere, both the

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[2] Stimuli are presented in the right- or left-visual-field with a tachistoscope or analogous computerized procedure. Connections between the hemispheres ensure that the information is not processed exclusively by the hemisphere to which it is initially projected.

frontal and temporal groups obtained negative difference scores[3], but the temporal lobe group displayed a greater relative verbal memory decrement. They did not compare raw test scores among the groups but, like Andrewes and colleagues (1990), they compared difference scores "in order to minimize variability due to individual differences and general level of efficiency" (Làdavas et al., 1979, p. 496). Their decision to compare difference scores makes it impossible to evaluate directly intergroup memory performances in the verbal and visual-spatial modalities, separately. Nonetheless, the results suggest a trend toward poorer verbal memory in left temporal patients and poorer visual-spatial memory in right temporal patients but no such pattern in the left and right frontal lobe groups.

Delaney et al. (1980) divided their patient groups according to "unequivocal" data and included only patients "for whom the medical evidence converged to a single, lateralized diagnostic category" (p. 105). Their findings indicated poorer immediate story recall performance in both LTL and RTL groups, and poorer delayed story recall and free recall of a fragmented word list performances in the LTL group, when compared to patients with a frontal lobe focus and normal controls. Delayed visual-spatial recall and visual recognition scores were lower for the RTL group when compared to LTL patients, patients with a frontal lobe focus, and normal controls. This study showed incomplete but consistent hemisphere-specific memory deficits, such that only the LTL group showed a verbal memory decrement and only the RTL group showed a visual-spatial memory decrement.

Summary. First, it appears that patients with TLE are particularly vulnerable to the type of memory deficits detected by standard tests when compared to patients with

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[3] An obvious typographical error in the presentation of the data (Làdavas et al., 1979, Table 5, p. 500) was corrected (using the data presented in Table 4, p. 499) to yield a negative LTM learning difference score for the left temporal lobe group.

frontal lobe epilepsy (Delaney et al., 1980), although some studies have failed to find a difference (Loiseau et al., 1983; Mirsky et al., 1960). Second, a number of studies have found material-specific interictal deficits in epilepsy patients with foci in the LTL or RTL that correspond to the deficits found in epilepsy patients with analogous post-surgical lesions. That is, a LTL focus was associated with a verbal memory deficit (Delaney et al., 1980; Giovagnoli & Avanzini, 1996; Tröster et al., 1989; Làdavas et al., 1979; Masui et al., 1984), and a RTL focus was associated with a visual-spatial memory deficit (Delaney et al., 1980; Làdavas et al., 1979). However, other studies have failed to find corresponding interictal deficits (Andrewes et al., 1990; Loiseau et al., 1983; Mayeux et al., 1980) or have found inconclusive results (Mungas et al., 1985; Rausch et al., 1978).

Methodological differences among studies with respect to patient characteristics, method of intergroup comparison, and choice of memory tests may underlie the discrepancies among these findings, at least in part. In addition, discrepancies may be related to imprecision connected with determining location of seizure focus. That is, the location of interictal spike activity does not invariably match the location of seizure onset or, when there is one, the location of a brain lesion (Halgren et al., 1991). Also, contralateral seizure activity, undetected by EEG, could affect memory performance (see Jones-Gotman, 1991). Furthermore, even a relatively well-defined unilateral temporal lobe focus group may remain rather heterogeneous because seizures could emanate from the medial, lateral, anterior, or posterior aspects of the temporal lobe (Thompson, 1991). In sum, large within group variability or substantial individual differences are likely present in epilepsy samples, even in the context of a significant group effect (e.g., Hermann, Wyler, Richey, & Rea, 1987).

Of the studies reviewed above, only three (Delaney et al., 1980; Làdavas et al., 1979; Mayeux et al., 1980) contained all of the following methodological characteristics:

a non-temporal lobe comparison group, adequate criteria for assigning patients to groups (i.e., at least interictal EEG), an attempt to account for at least some other variables that might influence for memory performance, and utilization of memory tests that covered both verbal and visual-spatial modalities and included delayed retrieval of newly learned information. Two out of these three studies found the expected material-specific memory deficits associated with unilateral TLE (Delaney et al., 1980; Làdavas et al.,1979). The study that found no inter-group memory differences (Mayeux et al., 1980) had small groups sizes, especially for the right temporal and generalized epilepsy groups (see Table 6).

Insert Table 7 about here

Epilepsy surgery candidates

As mentioned above, using interictal EEG results to determine the side of seizure focus will likely lead to some misassignment of patients. Such overlap among patient groups could mask actual effects due to side of seizure focus. In order to help overcome this problem, recent studies have employed epilepsy surgery candidates who have had the site of seizure focus estimated by a convergence of laboratory and clinical evidence including 24 hour video EEG, neuroradiological tests, and, in some cases, EEG with depth electrodes. In this section the review continues to examine the influence of the location of seizure focus on memory, but only studies that have employed candidates for epilepsy surgery will be included.

The studies in this section were all published since 1987, and they are all primarily interested in the memory performance of patients with right, left, or bilateral temporal lobe foci. This focus on TLE reflects the prevailing interest in the role of the

temporal lobes in memory functioning. It also reflects the preponderance of patients with temporal lobe foci who present as epilepsy surgery candidates (e.g., Breier et al., 1996). These patients provide a convenient population from which to select subjects for study. Because of their status as surgical candidates, neurological, radiological, laboratory, and neuropsychological assessment data are available. The drawback of exclusively using these patients is that they represent a highly selected sample from the general population of persons with epilepsy because their seizures are not well controlled by medication.

Four studies have examined the influence of LTL or RTL seizure onset on verbal memory in particular. Hermann and colleagues (1987) found that LTL patients displayed significantly poorer scores on selected measures of verbal memory than RTL patients and controls. However, Hermann, Seidenberg, Haltiner, and Wyler (1992a) found that, after accounting for the influence of demographic variables and language functioning in a multiple regression analysis, side of medial temporal lobe seizure onset was not a significant predictor of performance on a variety of verbal memory scores. Because language functioning (i.e., word finding) appeared to mediate verbal memory performance, this finding re-awakened the question of whether the poorer verbal memory displayed by LTL patients reflects a general retrieval inefficiency or a particular difficulty with storage and retrieval of newly learned information (see also Mayeux et al., 1980). To address this issue, Seidenberg et al. (1993) examined verbal recognition memory scores in more detail. They found that RTL patients were better able to discriminate between previously presented words and new words on a delayed recognition memory test than LTL patients. In addition, LTL patients displayed more errors of all types and more false positives than RTL patients. The authors concluded that

> these findings are consistent with the notion that the verbal learning impairments observed in left temporal lobectomy patients are not secondary either to impairments in access to and utilization of semantic

> memory information or to increased retroactive interference effects. Rather their recognition memory impairment appears to be associated with the inability to discriminate and retain individual items in long-term memory, a function which appears to be associated with hippocampal integrity (p. 199).

Finally, O'Shea, Saling, Bladin, and Berkovic (1996) found that both LTL and RTL patients performed more poorly on immediate story recall than primary generalized seizure patients. Also, the LTL patients performed more poorly than the other groups on the verbal paired associate learning test, but only when considering the most difficult word pairs.

Snitz, Roman, and Beniak (1996) attempted to establish a visual-spatial memory test that would "effectively lateralize to the right temporal lobe in presurgical epilepsy patients" (p. 753). They gave a measure of immediate and delayed visual-spatial recognition memory (the Continuous Visual Memory Test; CVMT) and a variety of other measures of verbal and visual-spatial memory for comparison (see Table 7). Contrary to expectation, visual-spatial recognition memory performance did not appear to discriminate between the patient groups after considering group differences in Full Scale IQ. Furthermore, this test did not correlate with other standard visual memory tests and appeared to measure visual-spatial processing rather than memory. In contrast, Delaney et al. (1980), using a test that was virtually identical to the acquisition phase of the CVMT (Recurring Figures Test of Kimura), successfully differentiated between non-surgical RTL and LTL patients using visual-spatial recognition memory scores. Helmstaedter, Pohl, Hufnagel, and Elger (1991) used a test that required reproduction of a list of line figures using wooden sticks over six learning trials. The RTL and bitemporal lobe (BTL) focus groups obtained poorer visual-spatial learning scores than LTL and normal control groups. The RTL group also made relatively more rotation errors on the task. The researchers' observations implied that verbalization of test items lead to

constructional errors. However, it was not reported whether RTL patients were more likely to use verbalization test strategies.

Other studies have examined both verbal and visual-spatial memory in a sample of epilepsy surgery candidates. Helmstaedter, Pohl, and Elger (1995) found that, when compared to normal controls, both RTL and LTL patients were impaired on verbal learning and recall of figures of varying complexity, and only left temporal lobe patients were impaired on verbal recall. However, when considering only the more complex visual-spatial items, the RTL group obtained poorer results than the LTL group. Furthermore, only in the RTL group was the verbal learning score correlated with visual-spatial retention, and, the correlation was due to the more complex items. These findings suggested that RTL patients tended to utilize a verbal strategy on the visual-spatial immediate recall test, and this strategy broke down when the items became too complex to be completely encoded. The results confirmed the speculations of Helmstaedter et al., (1991).

McGlone (1994) found that delayed verbal recall was poorer in patients with a LTL seizure focus than in patients with a RTL seizure focus. McGlone did not report whether there was an overall laterality effect on the delayed visual-spatial recall measure, but side of temporal lobe focus interacted with gender. RTL males displayed the expected visual-spatial recall decrement, but this effect was not seen in female patients. Similarly, Saykin et al. (1989) found that LTL patients displayed a relative verbal deficit, whereas RTL patients displayed no difference between verbal and visual-spatial memory.

Breier et al. (1996) attempted to predict location of seizure focus according to memory performance. Patients were divided into left temporal, right temporal, or extra-temporal groups according to the location of surgical intervention and, therefore, only those patients suitable for surgical intervention were included (see Table 7). The

researchers compared performances only on a subset of memory scores "that exhibited the largest group differences in comparison with other measures available" (p. 167). On delayed story recall both temporal groups performed more poorly than the extra-temporal group. On the last trial of a verbal learning test the left temporal group performed more poorly than the extra-temporal group. The results in the visual-spatial domain showed that performances on the last trial of a visual-spatial learning test and on two delayed visual-spatial recall tests discriminated between the right temporal and extra-temporal groups, with the right temporal group obtaining lower scores. There were no inter-group differences on verbal list learning or delayed word list recall. Finally, using memory scores, they were able to classify patients into their respective surgery groups with a 65% overall correct classification rate and sensitivites ranging from 57% to 75%. This indicated that despite a lack of entirely consistent material-specific memory findings when comparing patients with unilateral temporal lobe foci, memory performance can predict side of seizure focus in a significant number of epilepsy patients.

Jones-Gotman (1991) reported the memory performance of epilepsy surgery candidates who were divided into four groups according to side of subsequent temporal lobe excision and whether or not there were bilateral EEG abnormalities. On delayed verbal recall, both RTL groups outperformed both LTL groups, and patients with unilateral EEG abnormalities outperformed patients with bitemporal abnormalities. On delayed visual-spatial recall, the LTL patients with unilateral EEG abnormalities outperformed all of the three remaining patient groups. Thus, only the patients who had no detectable EEG abnormality in the RTL appeared to be unimpaired on delayed visual-spatial recall. This was the first published study to compare patients with unilateral versus bilateral EEG abnormalities when the suspected seizure focus was subsequently detected and removed.

Christianson, Nilsson, Säisä, and Silfvenius (1992) employed the visual half-field technique to evaluate memory functioning in TLE patients. They found that the recall performance of LTL patients was significantly poorer than normal controls, and patients with LTL epilepsy displayed a specific deficit recalling abstract words that were presented to the left hemisphere. Also, normal controls outperformed the LTL and RTL groups on verbal recognition memory. In an analogous study, random shapes were presented to each hemisphere. Normal controls outperformed both patient groups, and there was no effect for side of stimulus presentation. The authors concluded that the visual half-field technique was useful for discriminating between LTL and RTL patients when assessing verbal memory, but it was of little discriminative value when assessing visual-spatial memory. However, they failed to note that the significant effects found with the verbal memory test involved recall memory, whereas the visual-spatial memory test involved only recognition memory. Thus, it is possible that differences in test demands produced the significant effects, at least in part.

Two studies found no influence of temporal lobe seizure focus on memory performance. Thompson and Trimble (1996) found no differences between LTL and RTL groups on tests of verbal and visual-spatial learning, immediate and delayed recall, and recognition. However, they reported trends in the expected directions. Hermann, Connell, Barr, and Wyler (1995) found that the performances of LTL and RTL patients were equivalent on a test of recognition memory for faces and names. Recognition memory appears to be less sensitive to the effects of seizure focus than free recall. Neither of these studies employed a comparison group against which the patients' performances could be contrasted.

Summary. With regard to the studies employing epilepsy surgery candidates, it appears that there is a relationship between LTL seizure focus and verbal memory deficits

(Breier et al., 1995; Christianson et al., 1992; Helmstaedter et al., 1995; Hermann et al., 1987; Jones-Gotman, 1991; McGlone, 1994; O'Shea et al., 1996; Saykin et al., 1989; Seidenberg et al., 1993), although the nature of the verbal memory deficit may vary from study to study. Relatively few studies have failed to find a significant relationship between verbal memory and LTL focus (Hermann et al., 1995; Thompson & Trimble, 1996). RTL focus appears to be related to poor visual-spatial memory (Breier et al., 1995; Helmstaedter et al., 1991; Jones-Gotman, 1991), although some studies failed to find a relationship (Saykin et al., 1989; Snitz et al., 1996; Thompson & Trimble, 1996). It should be noted that the test used by Snitz and colleagues (1996) appeared to reflect visual-spatial skills rather than memory. Furthermore, the relationship between RTL and visual-spatial memory may be mediated by other factors. Helmstaedter et al. (1995) found that a deficit in immediate visual-spatial recall could be found in patients with RTL foci, but only when the items were too complex to be encoded efficiently using a verbal strategy. McGlone (1994) found that only RTL males displayed the expected visual-spatial recall decrement.

Two auxiliary points were raised in the above review. First, Jones-Gotman (1991) illustrated how EEG abnormalities contralateral to the presumed seizure focus can influence material-specific memory performance. Second, recognition memory does not appear to discriminate between patients with a LTL or RTL seizure focus (Christianson et al., 1992; Hermann et al., 1995)

Of the seven studies reviewed in which presurgical patients were employed, only the study conducted by Breier and colleagues (1996) contained all of the following methodological characteristics: a non-temporal lobe comparison group, adequate criteria for assigning patients to groups, an attempt to account for at least some other variables that might influence memory performance, and utilization of memory tests that covered

both verbal and visual-spatial memory and included delayed retrieval of newly learned information. The results of this study showed that the expected material-specific memory deficits were associated with unilateral TLE but only when the temporal lobe groups were compared with patients having extratemporal lobe foci. As in the studies employing non-surgical epilepsy samples, these results indicate that material-specific memory deficits corresponding to a LTL or RTL focus can be measured. Fortunately, the deficits are not typically severe. Comparing the performance of temporal lobe patients to extra-temporal lobe patients or controls seems to increase the likelihood of detecting a deficit.

Summary

More often than not, a relationship between unilateral temporal lobe focus and material-specific deficits has been reported in the published literature. This relationship appears to be more consistent among studies that employed epilepsy surgery candidates. This may be due to better methods of localizing seizure focus, or to the nature of this selected, chronic, and drug-resistant sample. A temporal lobe epileptogenic focus might have a detrimental effect on memory functioning because of the conditions that initiated the focus, or because of the consequences of recurring seizures.

The hippocampi are located adjacent to the medial aspect of the temporal lobes. They have been implicated as particularly important for memory storage and retrieval (Moscovitch, 1992). Recent studies have evaluated the particular role of the hippocampi in mediating memory performance in TLE patients. These results are described in the next section.

The relationship between hippocampal cell density and memory performance

The studies described in this section have investigated the particular mnestic role of the left and right hippocampi (see Table 8). All have used epilepsy surgery candidates

as participants. Of particular interest is the relationship between side of hippocampal pathology and material-specific memory performance.

Insert Table 8 about here

The correlation between left hippocampal volume and verbal memory in a group of newly diagnosed, unmedicated, LTL patients was examined by Kälviäinen et al. (1997). The left hippocampal volumes were significantly smaller in these patients compared to a control group, whereas the right hippocampal volumes were equivalent. Furthermore, the left hippocampal volume was correlated positively with measures of verbal memory. Whether "early structural and functional deficits are progressive and whether their severity influences the prognosis of epilepsy" remains to be evaluated (Kälviäinen et al., 1997, p. 286).

Sass et al. (1990) compared measurements of hippocampal cell density taken after epilepsy surgery to presurgical performance on verbal learning. Long term retrieval was correlated with pyramidal cell densities in particular areas of the hippocampus, but only in LTL patients. In addition, verbal learning performance was relatively low for both TLE groups compared with normative standards, and the LTL group obtained significantly lower performance than the RTL group. In a later study, Sass et al. (1992) found, as expected, that LTL patients displayed poorer verbal memory performance than RTL patients. Further results suggested that verbal retention was related to left sided hippocampal cell density, whereas naming and immediate and delayed story recall scores were related to LTL functioning "because these measures are more dependent upon the integrity of the patient's language skills, which are mediated by the neocortex" (p. 670). The percentage retained score might represent a more appropriate measure of memory

performance because, unlike the delayed recall score, it represents the amount of information that is retained during the delay interval. Other findings indicate that the loss of information during a delay interval is particularly sensitive to hippocampal damage (Frisk & Milner, 1990; c.f. McMillan, Powell, Janota, & Polkey, 1987).

Later research by Sass and colleagues (1995) also suggested that poor immediate story recall performance reflected cortical dysfunction within the left hemisphere, whereas a decline in the amount of verbal information retained during a delay and long term retrieval of a word list reflected left hippocampal dysfunction. These conclusions applied to TLE patients with or without structural cerebral lesions.

Rausch and Babb (1993), again consistent with previous findings, found that LTL patients obtained lower delayed verbal recall performance than RTL patients. Also, immediate and delayed recall of verbal paired associates were significantly related to low hippocampal cell density, but only in the LTL patients. In addition, the performance of patients with severely low hippocampal cell density was poorer than those with mild to moderately low hippocampal cell density. None of their remaining memory tests, including measures of delayed story recall and visual-spatial memory, was significantly related to hippocampal cell density. These researchers did not use a percent retention score in order to evaluate delayed recall independent of initial performance.

Lencz, in association with Sass and others (Lencz et al., 1992) demonstrated that MRI measurements can provide a fairly accurate estimate of hippocampal cell density. Also, they found that the relationships between memory performances and MRI were similar to previous studies examining the relationships between memory performances and hippocampal cell densities. Verbal retention was correlated with left hippocampal volume, but only in the LTL patients. Verbal learning, on the other hand, was correlated with LTL volume as well as LTL minus RTL ratio. The right hippocampal and RTL

volume measures did not correlate with any of the memory measures (verbal or visual-spatial; see Table 8).

A number of studies have categorized patients according to whether or not they displayed evidence of hippocampal sclerosis. McMillan and colleagues (1987) found that patients with hippocampal sclerosis performed relatively poorly on immediate and delayed story recall, regardless of the side of seizure focus. In contrast, among those who did not have hippocampal sclerosis, LTL patients performed more poorly on immediate and delayed story recall than RTL patients. In addition, there were no significant intergroup differences on delayed visual-spatial recall, or percent retained in either modality. The results suggested that both hippocampi were related to verbal memory performance in these epilepsy patients. It is notable, however, that estimated WAIS Verbal IQ and Performance IQ scores were both lower in the hippocampal sclerosis group than the group with other types of pathology and no attempt was made to evaluate how this might have been related to the story recall results (McMillan et al., 1987).

Miller, Muñoz, and Finmore (1993) found that patients with hippocampal sclerosis displayed poorer retention of visual-spatial information, relative to both the patients without hippocampal sclerosis and normal controls. Learning of word pairs was also relatively impaired in patients with hippocampal sclerosis, as well as in patients who later had LTL surgery. Patients with both a left temporal focus and hippocampal sclerosis performed relatively poorly on delayed recall of stories and word pairs. There were no side of focus effects for the visual-spatial memory tests or for the recognition memory tests in either modality. Thus, in contrast to McMillan et al. (1987), these results indicated that the presence of hippocampal sclerosis is associated with poor memory in both the verbal and visual-spatial domains, and the presence of both LTL seizure focus

and hippocampal sclerosis appeared to have a particularly detrimental effect on verbal recall.

Saling and colleagues (1993) found that patients with left hippocampal sclerosis performed more poorly than patients with right hippocampal sclerosis on learning of word pairs. There were no intergroup differences on story recall. In contrast, Baxendale and colleagues (1998) found patients with left hippocampal sclerosis obtained lower story recall scores than patients with right hippocampal sclerosis.[4] Furthermore, they found that left hippocampal volume predicted immediate story recall and right hippocampal volume helped predict delayed figure recall.

Baxendale, Cook, Shorvon, Thompson, & Warrington (1994, also described in Baxendale, 1995) found that patients with right sided hippocampal sclerosis displayed poorer verbal retention and produced more intrusions on a list learning task than patients with left sided hippocampal sclerosis. This result contradicted most previous research, however, it must be acknowledged that a percentage retained score is relatively unreliable (e.g., Coughlin & Hollows, 1985). Baxendale and colleagues also found that patients with anterior hippocampal volume loss performed more poorly than patients with diffuse hippocampal volume loss on a design learning test.

Summary

Research investigating the relationship between hippocampal cell density in TLE patients and memory functioning has been rather consistent. First, the findings provide further evidence that patients with a LTL seizure focus display a relative verbal memory deficit (McMillan et al., 1987; Miller et al., 1993; Rausch & Babb, 1993; Sass et al., 1990; 1992; 1995) although an analogous association between RTL seizure focus and

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[4] Saling et al. (1993) used the two WMS stories, whereas Baxendale et al. (1998) used the one AMIPB (i.e., Attention and Memory Information Processing Battery -- standardized in Britain) story for recall.

visual-spatial memory has not been supported (McMillan et al., 1987; Miller et al., 1993; Rausch & Babb, 1993). Second, the findings have begun to define the role of the hippocampus in memory functioning more clearly. Measures of left hippocampal volume or density in patients with LTL epilepsy were correlated with verbal memory in the expected direction (Kälviäinen et al., 1997; Lencz et al., 1992; Miller et al., 1993; Rausch & Babb, 1993; Sass et al., 1990; 1992; 1995). In contrast, right hippocampal volume or density in patients with RTL epilepsy was not related to a material-specific memory effect in any studies reviewed (Lencz et al., 1992; McMillan et al., 1987; Miller et al., 1993; Rausch & Babb, 1993) except one (Baxendale et al., 1994). Baxendale and colleagues (1994) found that patients with right hippocampal volume loss displayed poorer retention of a story than patients with left hippocampal volume loss. Notably, these authors did not report the side of temporal lobe seizure focus so one cannot evaluate the possible interaction between side of seizure focus and side of hippocampal volume loss. The only other significant effect regarding visual-spatial memory indicated that patients with anterior hippocampal volume loss performed more poorly than patients with diffuse hippocampal volume loss (Baxendale et al., 1994).

When patients were grouped according to the presence or absence of unilateral hippocampal sclerosis, the presence of sclerosis in either hippocampus was related to poor verbal recall (McMillan et al., 1987; Miller et al., 1993) but the result was less consistent with respect to visual-spatial retention (Miller et al., 1993; cf. McMillan et al., 1987). Finally, when comparing persons with left hippocampal sclerosis to persons with right hippocampal sclerosis, two studies found that left hippocampal sclerosis was related to poorer verbal memory performance (Saling et al., 1993, Baxendale et al., 1998) whereas two studies failed to find a difference (McMillan et al., 1987; Miller et al., 1993).

No study found intergroup differences on visual-spatial memory performance (Baxendale et al., 1998; McMillan et al., 1987; Miller et al., 1993).

Overall, previous findings suggest a critical interrelationship between the hippocampus and the LTL with respect to verbal memory functions. In addition, the findings of Sass and colleagues (1990; 1992; 1995) indicate that there may be a dissociation between the types of verbal memory tasks that are sensitive to LTL dysfunction versus left hippocampal dysfunction. In contrast, no interrelationship between the hippocampus and the RTL with respect to visual-spatial memory functions has been found. It should be noted, however, that the visual-spatial memory tests employed may not be sensitive enough to detect an effect.

Direct comparison of hippocampal integrity and presurgical memory performance has been undertaken only recently. Future research in this area commensurate with technical advances may help to define the relationship between the hippocampus and specific memory functions in more detail. In the next section, the review considers the relationship between other areas of cerebral pathology and memory functioning.

The relationship between cerebral pathology and memory performance

Many studies exclude patients with evidence of structural lesions with the rationale that they are interested in the effects of epilepsy in particular, not brain damage in general (e.g., Hermann et al., 1992a; Homan et al., 1989; Loiseau et al., 1980; 1983; Mayeux et al., 1980; O'Shea et al., 1996; Prevey, Delaney, & Mattson, 1988; Rausch et al., 1978; Sass et al., 1990; 1992; Scott et al., 1967; Seidenberg et al., 1993). However, Làdavas et al. (1979) were interested in the influence of structural lesions on memory performance. They found that the presence of clear evidence of structural lesions (via CT scan) did not influence their overall findings (previously described). The results suggested that structural lesions did not underlie memory disorders but, rather, the

electrical activity of the seizure focus was more important for determining memory outcome.

The previously described study by Sass and colleagues (1995) examined whether the verbal memory results of patients with TLE and no evidence of a brain lesion (other than hippocampal sclerosis) were similar to the results of patients with TLE and demonstrable evidence of a brain lesion. Indeed, the results were similar, and the presence or absence of a structural lesion in the temporal lobe appeared to have no effect on the correlations between verbal memory test performance and hippocampal cell counts in these patients. Also, long term retrieval was poorer for patients with LTL lesions when compared to patients with RTL lesions.

Other studies have investigated an association between dysfunction or damage in specific brain regions of persons with epilepsy and particular memory deficits (see Table 9). Homan et al. (1989) used the DSPECT technique to evaluate how regional cerebral blood flow (rCBF) might be related to memory performance. Using a stepwise discriminant function analysis they attempted to predict the location of rCBF abnormality from performance on various neuropsychological tests. The results indicated that immediate story recall score contributed to the prediction of rCBF in the left temporal or right frontal areas. Immediate visual-spatial recall score aided in predicting rCBF in the left frontal area, and delayed visual-spatial recall helped to predict rCBF in the left and right temporal areas. Delayed story recall did not help predict rCBF in any region. These findings are not entirely consistent with the material-specific memory deficits typically associated with particular seizure foci. Homan and colleagues offered no explanation for the discrepancies. Because of the way these authors chose to relate area of hypoperfusion and test performance, it is not possible to compare individual test performance among the left temporal, right temporal, left frontal, and right frontal hypoperfusion groups directly.

There were no significant correlations between the quantitative rCBF findings and memory test scores.

Insert Table 9 about here

Finally, Verhoeff et al. (1992) examined the relationship between memory and location of cerebral pathology in a unique way. They divided subjects according to the type and severity of memory impairment and judged location of cerebral pathology according to EEG, SPECT and CT results. Thirty-two percent of the patients showed detectable structural cerebral abnormalities. Their findings showed that global (i.e., both verbal and visual-spatial) memory deficits were associated with parietal lobe and frontal lobe pathology. The patients who did not fit into the global group (i.e., those who had only verbal impairment, only visual-spatial impairment, or no impairment) showed increased temporal lobe pathology. Neither the side EEG focus nor the SPECT findings were related to the type or severity of memory impairment. However, the sample size was small (i.e., only six and nine of the 28 patients showed EEG foci in the left and right hemispheres, respectively).

Summary

These studies have shown that particular memory deficits may help predict areas of hypoperfusion determined by DSPECT (Homan et al., 1989). In addition, one study found that material-specific memory deficits were more common among persons with temporal lobe pathology, whereas global memory problems tended to be associated with extra-temporal pathology (Verhoeff et al., 1992). On the other hand, other studies found that the presence of structural lesions had no apparent impact on memory outcome. Rather, the electrical activity of the seizure focus appeared to be more important (Làdavas

et al., 1979; Sass et al., 1995; see also Masui et al., 1984). Obviously, it would be necessary to consider the nature (e.g., size and location) of any structural lesion when attempting to determine how it may affect memory.

In the next section, a topic that has received copious attention with respect to cognitive effects is reviewed. That is, the research investigating the influence of various anticonvulsant drugs on memory performance in epilepsy patients is examined.

The effects of anticonvulsant drugs on memory performance

A large amount of research has been devoted to evaluating the effect of anticonvulsant drugs on memory functioning in epilepsy. This may be due in part to the fact that anticonvulsants represent one epilepsy variable that can be manipulated to a limited extent and measured relatively easily. Given the observations of memory deficits prior to the development of anticonvulsants, these drugs would not be expected solely to underlie the memory difficulties experienced by persons with epilepsy. However, they may provide part of the puzzle.

There are a number of reasons why it may be difficult to determine the independent effects of anticonvulsants on memory. First, the dosage and choice of drug often depend upon the type and severity of epilepsy (Kapur, 1994; see Table 4). Second, duration of exposure to anticonvulsants is related to duration of epilepsy, which may exert an independent effect on memory. Third, carbamazepine (CBZ) has been shown to have a positive effect on mood (Dodrill & Troupin, 1977; Robertson, Trimble, & Townsend, 1987; Thompson, 1991), and mood may influence performance on memory tests. Finally, anticonvulsants may interact with each other or with other medications to produce different effects.

A number of studies have attempted to assess the influence of anticonvulsants on memory performance in the context of examining the influence of other seizure-related

factors. They did not attempt to control anticonvulsant variables but, rather, correlated the type or amount of anticonvulsant to memory performance or compared groups differing in anticonvulsant drug regime. These studies will be described first, followed by the studies that were designed to examine the influence of anticonvulsants on memory more directly.

Correlational studies have failed to find a significant relationship between anticonvulsant serum level and memory performance (see Table 5; Loiseau et al., 1980; 1982; Rausch et al., 1978). Loiseau et al. (1983) found that taking monotherapy versus polytherapy had no effect on memory performance and there was no correlation between phenobarbitol (PB), phenytoin (PHT), or valproic acid (VPA) monotherapy and memory test scores.[5] Homan et al. (1989) found no differences among patients taking zero, one, two, or three anticonvulsant drugs on immediate and delayed recall.

Other studies have looked more specifically at type of anticonvulsant drug. Verhoeff et al. (1992) found no relationship between type of anticonvulsant (including CBZ, PHT, and VPA) and delayed recall.[6] Delaney et al. (1980) found no effect of PHT on a variety of memory tests, and PB was positively correlated with only one memory variable: immediate figural recall.

Experimental and quasi-experimental studies are summarized in Table 10. Thompson and Trimble (1981) compared the performance of patients who had had a reduction in anticonvulsant therapy versus patients who had had no change in their anticonvulsant therapy. They found that delayed picture recall improved after anticonvulsant reduction, but five other memory tests were unaffected. In a later study by Thompson and Trimble (1983), patients were tested before and after their anticonvulsant

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[5] They did not present statistical results to support these findings.

[6] They did not present statistical results to support this finding.

drug levels were either raised or lowered. There was no effect of anticonvulsant serum level on delayed memory, whereas relatively high anticonvulsant serum levels were related to poorer performance on measures of immediate recall. When a subset of the patients were removed from the sample because their serum anticonvulsant drug levels were in the biochemically toxic range, the results changed somewhat. The relatively high anticonvulsant level group performed more poorly on the immediate and delayed word recall tests, but there was no difference on the picture recall tests. This change in results is difficult to interpret for the researchers did not report the specific characteristics of the patients who were excluded, other than their anticonvulsant levels. Nevertheless, the authors agreed that the significant results indicating poorer memory performance with high anticonvulsant drug level were most likely due to concomitant decrements of concentration and mental speed.

Insert Table 10 about here

Other studies have investigated the effect of changing patients from polytherapy to monotherapy. Prevey et al. (1989) found that, after a change to VPA monotherapy, patients with uncontrolled idiopathic seizures showed no significant change on a number of memory tests, despite improvements in attention / concentration and mood. In contrast, Ludgate, Keating, O'Dwyer, and Callaghan (1985) found that patients produced fewer errors on a measure of visual-spatial retention after a change to monotherapy. Also, their Performance IQ and concentration performance improved. No other memory tests were employed.

The effect of CBZ on memory performance in epilepsy patients has been examined in a number of studies. Trimble and Thompson (1983) found no effect of CBZ

serum level on recall and recognition memory tests. However, the sizes of their patient groups were very small. Pulliainen and Jokelainen (1994) randomly assigned two different anticonvulsants to newly diagnosed epilepsy patients and tested them before commencement of treatment and after 6 months. CBZ produced no significant change on a variety of memory tests. Indeed, Thompson and Trimble (1981) showed that performance on measures of immediate and delayed recall and delayed recognition of pictures and words improved after patients' anticonvulsant levels were reduced or withdrawn and CBZ was added to their treatment. They did not assess concentration or IQ performance.

The effect of PHT on memory performance in epilepsy patients was also examined in the study by Pulliainen and Jokelainen (1994) described above. They found no significant change in memory performance after 6 months of PHT treatment. However, these patients failed to show the practice effect displayed by normal controls and patients taking CBZ on visual-spatial memory.[7] Trimble and Thompson (1983) found no effect of PHT serum level on five memory tests, but, they found that patients with relatively high serum concentrations of PHT displayed poorer performance on a measure of immediate recall of pictures. They also displayed deficits on measures of attention and motor speed. Thus, the significance of the isolated memory effect may have been related to other cognitive factors. In addition, the sizes of their patient groups were very small.

Sommerbeck et al. (1977) found that VPA, added to original anticonvulsant therapy, had no effect on verbal paired associate learning in a heterogeneous group of patients who were previously therapy-resistant. Also, Trimble and Thompson (1983) found no effect of VPA serum level on five memory tests, but, patients with relatively

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[7] There was no measure of immediate and delayed verbal recall for comparison.

high serum concentrations of VPA displayed poorer performance on a measure of immediate recall of pictures. These results are similar to those found with PHT noted above; the isolated memory effect may have been related to other cognitive factors and the sizes of their patient groups were very small.

Other studies have compared the performances of patients receiving different anticonvulsants without reference to a change in anticonvulsant level. Andrewes, Tomlinson, Elwes, and Reynolds (1984) found no differences between groups taking either PHT or CBZ monotherapy on a number of memory tests. Meador, Loring, Huh, Gallagher, and King (1990) employed a double-blind triple crossover design using CBZ, PB, and PHT and found no significant differences between the drug groups on a verbal learning test. In contrast, Andrewes, Bullen, Tomlinson, Elwes, and Reynolds (1986) found that patients taking CBZ monotherapy showed better performance on selected verbal memory tests than patients taking PHT monotherapy, suggesting only subtle differences in memory performance between the groups. The CBZ group were also superior on a short term memory scanning task.

Unlike the studies described thus far, in which it had been necessary for the epilepsy patients to maintain at least minimum anticonvulsant therapy, a series of studies by Gallassi and colleagues (Gallassi et al., 1986; Gallassi et al., 1987; Gallassi et al., 1988; Gallassi et al., 1992) employed epilepsy patients who had been seizure free for a minimum of two years and were undergoing a controlled withdrawal of their medication. They found that withdrawal of CBZ (Gallassi et al., 1986, 1988, 1992), PHT (Gallassi et al., 1987, 1988, 1992), PB (Gallassi et al., 1986, 1992), and VPA (Gallassi et al., 1992) produced no demonstrable effect on learning a series of digits or a visual-spatial sequence. They did not measure delayed recall.

Finally, Durwen and colleagues (Durwen, Hufnagel, & Elger, 1992; Durwen & Elger, 1993) assessed candidates for epilepsy surgery at full anticonvulsant level and when anticonvulsant level was reduced to increase the probability of videotaping a seizure. In the 1992 study they assessed 13 patients with LTL foci and found that, while other verbal memory measures were unaffected by anticonvulsant level, susceptibility to retroactive interference[8] (RI) was increased at full anticonvulsant level. This suggested increased susceptibility to verbal RI in these LTL patients when taking anticonvulsants as prescribed. In the 1993 study Durwen and Elger attempted to replicate this finding using both LTL and RTL patients. They found the same effects on verbal recall after a short delay during which an interfering word list was presented, but only in the LTL group. The RTL group showed no change in verbal memory performance after a reduction in anticonvulsant levels. Durwen and colleagues speculated that "epileptogenic neurons in the temporal network of memory function may be particularly susceptible to medication effects. The generation of seizures may be suppressed by medications, but on the other hand there may be also a very strong inhibitory influence on those regular physiological functions that may still take place within the epileptogenic area" (Durwen & Elger, 1993, p. 6). In addition, "It seems most likely that these phenomena are general effects of all anticonvulsant drugs" (Durwen & Elger, 1993, p. 6).

These findings lead to the question: Is a memory deficit associated with specific seizure foci related to the epileptogenic activity in that focus or to the suppression of activity due to anticonvulsant drugs? In order to answer this question, patients who have their epileptogenic activity suppressed by anticonvulsants would have to be compared with patients who do not have epileptogenic activity suppressed. Due to obvious ethical considerations, this comparison cannot be carried out.

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[8] i.e., recall of a target word list after a short delay during which an interfering word list was presented.

The studies by Durwen and colleagues illustrated a previously unstudied issue. That is, anticonvulsant effects on particular memory parameters might be found only in specific patient subtypes. Thus, it is possible that anticonvulsants can affect particularly vulnerable aspects of memory performance in specific patient subtypes (e.g., verbal RI in LTL patients). If this were the case, then a real anticonvulsant effect might be overlooked when assessing in a heterogeneous sample of patients.

Summary

The results of studies that examined the correlation between anticonvulsant drugs and memory functioning have found no detrimental effects due to the use of anticonvulsants (Delaney et al., 1980; Homan et al., 1989; Loiseau et al., 1980; 1982; 1983; Rausch et al., 1978; Verhoeff et al., 1992). Anticonvulsant drugs have been shown to produce more consistent deficits in other cognitive functions such as attention, concentration, and motor speed (Dodrill & Temkin, 1989; Duncan, Shorvon, & Trimble, 1990; Trimble & Thompson, 1983; for reviews see Bennett, 1992; Smith, 1991). These effects appear to be largely independent of memory functioning per se, although they can underlie memory deficits (Thompson & Trimble, 1983).

Nonetheless, selected memory deficits have been related to high anticonvulsant serum level, in the context of concomitant decrements of concentration and motor speed (Thompson & Trimble 1981; 1983). A change from polytherapy to monotherapy was consistently associated with improvements in attention and concentration, although the results with respect to memory performance were mixed (Ludgate et al., 1985; Prevey et al., 1989). Studies that have attempted to evaluate the effects of individual anticonvulsants on memory have found few differences (Andrewes et al., 1984; Meador et al., 1990; Pulliainen & Jodelainen, 1994; Sommerbeck et al., 1977; Trimble & Thompson, 1983). Though, in comparison with other anticonvulsants, patients receiving

CBZ have shown superior performance on selected memory tests, as well as superior performance on attention and concentration (Andrewes et al., 1986), whereas patients receiving PHT (Andrewes et al., 1986; Pulliainen & Jodelainen, 1994; Trimble & Thompson, 1983), and high levels of VPA (Trimble & Thompson, 1983) have shown subtle performance declines. Finally, the studies by Durwen and colleagues (Durwen et al., 1992; Durwen & Elger, 1993) indicate that particular effects due to anticonvulsant level may be found only in specific patient subtypes.

In the next section, the review shifts from a focus on neurobiological factors to a focus on other cognitive factors that may be related to memory performance in persons with epilepsy. It is important to evaluate the integrity of other cognitive functions when assessing memory because deficits in other areas, such as attention and language, can adversely affect memory test performance.

Other Cognitive Factors

The relationship between other cognitive functions and memory performance

Performance on a memory test depends upon a number of cognitive functions including the initial sensation and perception of incoming information, adequate attentional capacity, storage capability, retrieval capability, and response capability. Thus, when an individual obtains a poor performance on a memory test, it needs to be understood what event or events during the memory process has or have broken down. With regard to the memory performance of epilepsy patients, impaired language and verbal functioning, visual-spatial skills, attention and concentration, metamemory, and strategy use have been regarded as potential underlying factors associated with memory complaints or poor performance on memory tests. In this section studies that have

investigated the relationship between these cognitive variables and memory performance in epilepsy patients are reviewed (see Table 11).

Insert Table 11 about here

General intellectual level

Most studies of memory functioning in persons with epilepsy have examined IQ only to establish that it is equivalent across participant groups. Also, most studies exclude patients with IQs below 70, presumably to control for the influence of general intellectual deficiency on memory test performance.

No significant group differences in IQ level have been found when comparing LTL to RTL patients (Breier et al., 1996; Christianson et al., 1992; Giovagnoli & Avanzini, 1996; Helmstaedter et al., 1991; Hermann et al., 1992a; 1995; Mayeux et al., 1980; Miller et al., 1993; O'Shea et al., 1996; Sass et al., 1995; Thompson & Trimble, 1996), or when comparing TLE to other types of epilepsy (Breier et al., 1996; Mayeux et al., 1980; O'Shea et al., 1996), among studies investigating memory functioning. Indeed, when persons with epilepsy are compared to normal controls, IQ differences typically are not found (Christianson et al., 1992; Giovagnoli & Avanzini, 1996; Helmstaedter et al., 1991; Loiseau et al., 1984). One study found that TLE patients with hippocampal sclerosis had lower IQ scores than patients with other types of pathology (McMillan et al., 1987), although another study found no IQ differences among persons with epilepsy who either did or did not have hippocampal sclerosis (Miller et al., 1993).

IQ is related to many measures of memory in normals (e.g., WMS-R, Wechsler, 1987), but this relationship may not be as straightforward in persons with epilepsy. For example, memory differences occur between patient groups in the absence of IQ

differences between groups (Breier et al., 1996; Christianson et al., 1992; Giovagnoli & Avanzini, 1996; Helmstaedter et al., 1991; Loiseau et al., 1984; Miller et al., 1993; O'Shea et al., 1996; Sass et al., 1990; Schwartz & Dennerll, 1969; Seidenberg et al., 1993). Only one study found the opposite effect; that is, differences among epilepsy groups were not found on memory test scores but they were found on IQ test scores (Stevens et al., 1972). Also, Rausch et al. (1978) found that extent of spike activity was negatively correlated with IQ, whereas degree of lateralization of spike activity was not correlated with IQ. Conversely, WMS MQ was positively correlated with degree of lateralization but not correlated with extent of spike activity.

More direct evidence that the relationship between IQ and memory is different in epilepsy patients than in normals is provided by Loiseau et al. (1984), who found that IQ and learning and memory performance were significantly correlated in a group of normal controls, but not correlated in a group of persons with epilepsy. Similarly, other studies have found no correlation between IQ scores and memory test performance in persons with epilepsy (Dodrill, 1986; Seidenberg et al., 1993; Thompson & Trimble, 1996).

Schwartz and Dennerll (1969) found no FSIQ differences among groups of patients. However, they found that the patient group with both grand mal and psychomotor seizures had the poorest visual-spatial recall scores, and it was the only group that did not display a significant positive correlation between IQ and memory performance. Similarly, Sass et al. (1995) found LTL patients obtained lower long term retrieval scores and did not display a significant correlation between FSIQ and long term retrieval. In contrast, FSIQ and long term retrieval were correlated in the RTL lesion group. Again, the pattern emerged in which the group that showed a memory deficit did not show a correlation between IQ score and score on the deficient memory test. These

results are consistent with the idea that IQ level is not related to memory performance when a memory deficit exists.

Mirsky et al. (1960) found that WMS MQ was positively correlated with Full Scale IQ. Also, their generalized group had lower IQ and MQ scores as well as higher frequency of seizures than the temporal and frontal groups. Their results suggested that relatively low general intellectual level could have accounted for the memory deficit evident on the WMS. In addition, a third factor, seizure frequency, could have underlain both cognitive deficits.

Verbal IQ

Given the overlapping verbal skills involved, one might expect Verbal IQ level and verbal memory performance to be correlated. However, the results of a number of studies indicate that Verbal IQ score is not related to verbal memory deficits in persons with epilepsy. For instance, Hermann and colleagues (1988) found that Verbal IQ did not predict verbal memory deficit in LTL patients. Other studies that examined the relationships among hippocampal cell density, Verbal IQ, and verbal memory, found that hippocampal volume was significantly associated with verbal memory but unrelated to Verbal IQ (Rausch & Babb, 1993; Sass et al., 1990). This pattern suggested that the left hippocampus played an important role in verbal memory that was independent of general verbal functioning. However, Rausch and Babb (1993) also found that LTL patients had both lower Verbal IQ scores and lower verbal memory scores than right temporal patients.[9] Perhaps these concurring deficits reflected dysfunction in both the LTL and the left hippocampus.

Sass et al. (1992) found that level of performance on a story recall test was related to Verbal IQ level in TLE patients. However, the proportion of the story retained during

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[9] There were no differences with respect to FSIQ or PIQ.

a delay was not related to Verbal IQ. In addition, story recall and Verbal IQ were not related to hippocampal neuron loss, whereas proportion retained was correlated with hippocampal neuron loss. The results suggested that percent retained was independent of Verbal IQ, but level of performance on a prose recall test was related to Verbal IQ level. Percent retained may represent a more "pure" measure of memory.

Tomlinson, Stirling, Merryfield, and Reynolds (1981) found relatively poor scores on both delayed word recognition and estimated Verbal IQ in a heterogeneous epilepsy sample. They did not report the degree to which estimated Verbal IQ and delayed word recognition were correlated. Instead, they used ANCOVA and found that the difference between the epilepsy group and normal controls on word recognition disappeared after the effect of Verbal IQ was partialled out. However, this finding does not necessarily indicate that the difference in delayed word recognition performance was due to the difference in estimated Verbal IQ score. For example, if lower Verbal IQ is related to having epilepsy, then partialling out its effect might serve to eliminate part of the variable of interest by artificially compensating for the effects of epilepsy. Thus, ANCOVA is often not an appropriate method for providing statistical control over differences between groups in neuropsychological research (see Adams, Brown, & Grant, 1985).

Language functioning

As a group, persons with epilepsy display a relatively high level of language difficulties, especially with respect to expressive language (Thompson & Trimble, 1996). Further, a number of studies have shown that language functioning is correlated with traditional measures of verbal memory in epilepsy (e.g., Hermann et al., 1988; Mayeux et al., 1980). Thus, it is important to consider the presence of language deficits before drawing conclusions about verbal memory functioning.

The study by Mayeux et al. (1980), described previously, showed that naming performance was correlated with immediate story recall performance in LTL patients. However, whereas these patients displayed naming deficits, they did not display memory deficits. Hermann et al. (1988) found that confrontation naming and word fluency were the best overall predictors of verbal memory performance in LTL patients; none of the remaining nine neurobiological, cognitive, or psychosocial variables were significant predictors of verbal learning and recall (see Table 11). In a later study, Hermann et al. (1992a) assessed both LTL and RTL patients and found, similarly, that language performance was a significant predictor of verbal memory performance. In addition, patients with poorer naming scores performed more poorly on selected verbal memory measures (i.e., short delay free recall, learning slope, recall intrusion errors, and secondary list recall) than patients with higher naming scores, regardless of site of seizure onset.

As naming, word fluency, and memory test performance all require retrieval of words, it is possible that the association between language and verbal memory deficits is due to an impaired general retrieval capability (Hermann et al., 1988). A study by Seidenberg et al. (1993) attempted to evaluate how the memory and naming deficits sometimes displayed by persons with TLE both might be related to a general inefficiency in retrieving stored information. They examined qualitative performance on a verbal recognition task and found recognition memory impairments in the LTL patients relative to the RTL patients "to be associated with the inability to discriminate and retain individual items in long-term memory" (p. 199). These results indicated that the verbal memory deficit associated with LTL epilepsy was at least partially independent of language deficits. It appeared that a deficit in language functioning could account for

verbal memory deficits in epilepsy patients, but this was not likely the sole mediating factor.

Further research has indicated that language functioning appears to be related to only specific aspects of verbal memory performance (O'Shea et al., 1996). For instance, Sass et al. (1992) found that level of performance on a story recall test was correlated with naming performance in LTL patients, but the proportion of the story retained during a delay was not related to naming. Similar to the Verbal IQ results, percent retained appears to be independent of naming skill and it may represent a relatively "pure" measure of memory performance. In a similar vein, Hermann et al. (1988) found that four indices of verbal memory performance were correlated with language impairment in patients with dominant (i.e., usually left) TLE. However, the RI index (i.e., change in recall performance after presentation of an alternate word list) was not correlated with language impairment.

Visual-spatial skills

No published studies have directly evaluated the influence of visual-spatial skills on visual-spatial memory performance in epilepsy patients. However, a few studies have provided hints regarding the relationship between visual-spatial skills and memory. Dodrill's (1986) data showed that the mean performances of patients with generalized seizures on four Performance scale subtests of the WAIS[10], on a measure of construction dyspraxia, and verbal recall were within normal limits. Helmstaedter et al. (1991) found that performances on a visual-spatial skill task and on the first and last trials of a visual-spatial learning test were lower for RTL and BTL groups than a LTL group. However, in contrast, the only significant difference in mean learning performance showed the LTL

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[10] including Picture Completion (detecting visual detail), Block Design (assembling blocks to form a design), Picture Arrangement (assembling a series of pictures into the correct sequence), and Object Assembly (assembling puzzle pieces to form an object).

group lower than the normal controls. The RTL group made the most incorrect rotations and the LTL and BTL groups made more incorrect rotations than the normal controls. They did not report the correlation between visual-spatial learning and skill scores. Rather, they applied an ANCOVA to adjust the memory test scores by partialling out the effect of visual-spatial skill and the results remained significant. Another ANCOVA was conducted in which the visual-spatial skills scores were adjusted by partialling out the effect of memory test performance. The intergroup differences due to visual-spatial skill disappeared after this adjustment. However, as previously described, ANCOVA has been shown to be an invalid method of controlling for intergroup differences on an independent variable (Adams et al., 1985). Indeed, if taken at face value, these results suggested that memory test performance underlied visual-spatial skill performance whereas visual-spatial skill did not underlie visual-spatial memory performance. This seems illogical because the performance requirements of the visual-spatial skill measure do not place any obvious demands on memory storage or recall. Thus, one cannot make firm conclusions regarding the effect of compromised visual-spatial skill on visual-spatial memory performance in epilepsy patients based on these data. However, the patient groups were relatively impaired on both measures as well as attention.

Finally, Ludgate et al. (1985) found that patients produced fewer errors on a measure of visual-spatial retention after a change to monotherapy. However, their performances also improved on three subtests of the WAIS Performance IQ scale[11]. There was no control group employed to rule out improvements due practice effects, although no improvements were noted on the eight remaining WAIS subtests. These results highlighted the importance of considering the adequacy of visual-spatial skills before evaluating visual-spatial memory.

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[11] Digit Symbol (speeded copying of coded symbols), Block Design, and Object Assembly.

Attention and concentration

If attentional capacity or concentration is compromised it can have a detrimental effect on memory performance. That is, if an individual has difficulty attending to a stimulus it will be more difficult to store it. Similarly, if an individual has difficulty concentrating on a memory task it may become more difficult to retrieve the required information. Thus, it is important to consider a person's attentional capacity and mental efficiency when making judgements about memory performance. Despite these observations, surprisingly few investigations of memory functioning in epilepsy have reported patient performance on an independent measure of attentional capacity.

The cognitive process called attention consists of at least three components: alertness, selectivity, and processing capacity (Posner & Boies, 1971). Within the context of a clinical neuropsychological assessment, attention is commonly measured by tests of vigilance, short-term storage capacity, mental tracking, or complex attentional skill (Lezak, 1995). Measurements of attention performance in studies investigating memory functioning in epilepsy patients have included vigilance and mental tracking.

As mentioned earlier, it has been found that anticonvulsants can produce significant deficits in attention and concentration (for reviews see Bennett, 1992; Smith, 1991). These effects appeared to be largely independent of memory functioning per se, although they could underlie memory deficits. For example, in the study described earlier by Thompson and Trimble (1983), it was concluded that the few poorer memory test results displayed by the high anticonvulsant group were most likely due to concomitant decrements in concentration and mental speed. However, they did not attempt to examine the correlation between concentration and mental speed and memory performance. Similarly, Ludgate et al. (1985) found that visual-spatial memory improved

after anticonvulsant reduction, but performance also improved on measures of Performance IQ and concentration.

Dodrill (1986) obtained scores on the Stroop test[12], the Trail Making Test[13], and the Arithmetic[14] and Digit Symbol subtests of the WAIS, and immediate story and visual-spatial recall in a group of patients with tonic-clonic seizures of varying frequency. When compared to normative data, clinically significant impairments were not apparent in attention or memory when considering the mean scores of these patients (see Dodrill, 1978; Reitan & Wolfson, 1993; Wechsler, 1945). However, the high seizure frequency patients, on average, showed a clinically relevant impairment on the Stroop test whereas their performance on the memory tests was in the average range. This constrasting result suggests that attentional difficulties can occur without concomitant deficits on memory tests in epilepsy patients. Dodrill did not attempt to correlate performance on these tests with memory performance directly.

Helmstaedter et al. (1991) found that TLE patients had both lower attention and visual-spatial learning scores than controls. They did not report the correlation between learning and vigilance scores, but they applied an ANCOVA to adjust the memory test scores by partialling out the effect of attention performance. This analysis remained significant. However, as previously described, ANCOVA can be an invalid method of controlling for intergroup differences on an independent variable (Adams et al., 1985). Therefore, it cannot be said unequivocally that the lower memory performance in these patients was not related to an attentional deficit.

Loiseau et al. (1984) conducted a study that was specifically designed to compare attention and memory test performance. Total learning and recall scores were lower in

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[12] A measure of selective attention and ability to inhibit automatic responses.

[13] A measure of sequencing, mental flexibility, and psychomotor speed.

[14] A measure of mental arithmetic speed.

patients with generalized seizures and total attention score was lower in both generalized and partial seizure groups compared to controls. Remarkably, the results indicated no significant linear correlation between memory performance and attention or IQ in these epilepsy patients, but these correlations were significant in a normal control group. The results were based on a small sample size and were considered preliminary. Nevertheless, it appeared that the relationship between attention and memory performance found in normals was not present in epilepsy patients.

Metamemory and strategy use

A survey on the use of "memory aids" or mnemonic devices in persons with epilepsy indicated that normal control subjects used calendars, shopping lists, mental retracing, and first-letter cueing more often than persons with epilepsy (Thompson, 1991). The reason for this discrepancy may be related to an underlying deficiency in the ability to apply strategies to overcome the common shortcomings of human memory. Also, epilepsy patients may tend to have caregivers, friends, or family members who act as "memory aids" for them. Only the first explanation has been investigated empirically.

The results of a number of studies have indicated that epilepsy patients may approach memory tasks differently than normal controls. For example, TLE patients may be unable to benefit from a "feeling of knowing" to guide their guessing strategy on memory tests (Prevey et al., 1988). Also, an examination of verbal recognition indicated that LTL patients tended to guess "yes" more readily than RTL patients (Seidenberg et al., 1993).

Powell and colleagues (Powell, Sutherland, & Agu, 1984) examined the proportion of words recalled at each serial position during a word list learning task. They found, contrary to expectation, that persons with epilepsy tended to show poorest performance at the last two serial positions when compared to controls. The researchers

proposed that the persons with epilepsy had rehearsed earlier items at the expense of later ones. To test this hypothesis, they gave patients with temporal lobe involvement (two-thirds of whom had epilepsy) two different versions of the test: one listening to the word lists and one reading the word lists. The latter was introduced to prevent the patients from rehearsing the earlier words. In the reading condition, the number of words recalled at serial positions one to five decreased and the number of words recalled at serial positions six to ten increased. Powell et al. (1984) suggested that epilepsy patients displayed "low risk-taking in a group often aware they have memory problems" (p. 154). This study did not investigate whether the strategy of these patients impaired their overall performance on the memory tests. However, if further research could show that persons with epilepsy selectively attend to initially presented information at the expense of later information, this tendency could be related to differences in memory performance.

A study by Prevey and colleagues (1988) evaluated metamemory performance in TLE patients. They found no difference between patients and controls when they were asked to estimate the number of digits or figures they could repeat correctly. However, actual patient performance was significantly poorer than control performance. They concluded that patients tended to overestimate their immediate recall span (even though they did not test this hypothesis directly by examining the difference between the participants' estimated and actual performance). In a second study these researchers measured "feeling of knowing" in a general knowledge test. They found that TLE patients were less accurate than controls at predicting that they could pick the correct answer, but equally as accurate at predicting that they could not pick the correct answer. Consistent with the first study, these results indicated that the epilepsy patients tended to overestimate their memory abilities. It should be noted that the participant groups were equated on demographic and seizure-related variables but they were not equated on

cognitive variables such as IQ. Furthermore, the epilepsy patients showed a poorer fund of general knowledge than the controls. Thus, differences in retrieval ability or another variable such as general intellectual functioning might have underlain the poor metamemory performance shown by the patients. A later study by Prevey, Delaney, Mattson, and Tice (1991) found that control subjects' perceived feeling of knowing was related to how quickly they could recognize correct answers on general knowledge questions but TLE patients did not display this relationship.

Delaney, Prevey, and Mattson (1982) found that TLE patients made marginally fewer errors of omission (failure to recall an item) than controls and significantly more perseverative errors (prior item intrusions) than controls using the Peterson short term memory paradigm. The authors suggested that this "trade-off" may have reflected increased susceptibility to proactive interference on the part of persons with TLE. Yet, it is also plausible that the patients were more likely to guess, using a previously presented item, than not to answer at all. That is, the patients may have been "trying harder" to make sure that they provided three responses per trial, even if their answers came from previously presented trials. Moreover, if these patients had difficulty utilizing a "feeling of knowing" in order to guide their guesses (Prevey et al., 1988), they may have been more likely to invoke a previously presented word. These ideas remain to be explored.

Research with post-operative patients has indicated that frontal lobe lesions can be related to poor delayed list recall when patients are not instructed to use a retrieval strategy or when there is interference at retrieval (Incisa della Rocchetta & Milner, 1993). Moreover, the frontal lobes have been associated with the strategic processes important for successful performance on an unstructured recall task such as recalling a list of unrelated words (Moscovitch, 1992). In the study by Breier et al. (1996), described earlier, delayed recall of a word list was the only memory measure out of six on which

the extratemporal lobe patients (65% of whom had frontal lobe foci) did not outperform temporal lobe patients. It is possible that the extratemporal lobe patients performed relatively poorly on this test because of difficulty implementing an appropriate strategy. Breier et al. (1996) did not evaluate the strategic approach used by the patients but it would be interesting to relate the strategic approach used by patients with different seizure foci, especially foci in the frontal lobes, to memory performance.

Comment on the RI index

The RI index is computed on a word list learning task as the difference between the number of words recalled on the last learning trial and the number of words recalled from the same word list after an brief interval during which an interfering word list was presented. Hermann et al. (1988) found that RI was the only index on a verbal list learning and recall test that was not correlated with demographic, seizure related, verbal IQ or language impairment variables in LTL patients. These findings raised "the possibility that this index might serve as the best pure indicator of memory function in dominant temporal lobe patients" (p. 251). Durwen and colleagues (Durwen et al., 1992; Durwen & Elger, 1993) found that the RI index was the only parameter on a verbal list learning and recognition test that was affected by anticonvulsant levels in LTL patients. Thus, the RI index may be an important and sensitive measure of memory dysfunction which is relatively independent of other cognitive functions, especially in LTL patients.

The RI index does not appear to reflect verbal skills, but how well does it correlate with other memory indices? Wiens, Tindall, and Crossen (1994) factor analysed the CVLT in a sample of 700 successive job applicants and found seven factors. The RI index loaded on the seventh factor, and none of the other 21 indices loaded on this factor. This factor was called the retroactive/short-delay effect. The remaining six factors were named: general verbal learning, response discrimination, learning strategy, proactive

effect, acquisition rate factor, and serial position effect. In the original CVLT normative study (Delis, Kramer, Kaplan, & Ober, 1987) the RI index loaded on the general verbal learning factor in a group of 286 normal subjects, but in a sample of neurological patients it yielded a separate factor equivalent to the Wiens et al. (1994) data. Contrary to the Durwen findings, Delis et al. (1987) speculated that neurological patients may show less RI because they often respond to each trial during a word list learning test as though it were a new list. In any case, it would appear that the RI index represents a process that is relatively independent of six memory-related factors, as well as verbal IQ and overall language impairment scores in epilepsy patients. Thus, it would be valuable to consider this variable when trying to evaluate memory performance independent of other cognitive factors.

Summary

Previous research has indicated that FSIQ (Dodrill, 1986; Loiseau et al., 1984; Sass et al., 1995; Schwartz & Dennerll, 1969; Seidenberg et al., 1993; Thompson & Trimble, 1996; cf. Mirsky et al., 1960) and attention and concentration skills (Dodrill, 1986; Helmstaedter et al., 1991; Loiseau et al., 1984) are not significantly related to memory performance in persons with epilepsy, especially when memory deficits are present. However, these skills were found to be significantly correlated in normals (Loiseau et al., 1984). Verbal IQ and verbal memory scores appear to be unrelated in epilepsy patients (Hermann et al., 1988; Rausch & Babb, 1993; Sass et al., 1990; cf. Tomlinson et al., 1981). However, on a prose recall test Verbal IQ may be related to the total amount of information recalled but independent of percent of information retained during a delay, the latter measure being more uniquely related to memory (Sass et al., 1992). The possible relationship between visual-spatial skills and visual-spatial memory performance in epilepsy patients remains to be investigated. Epilepsy patients appear to

display poorer metamemory and use of strategy than control subjects (Powell et al.,1984; Prevey et al., 1988; 1991; Seidenberg et al., 1993).

Language skills, especially object naming performance, appear to be significantly related to performance on standard verbal memory tests in persons with epilepsy (Hermann et al., 1988; 1992a; Mayeux et al., 1980; Sass et al., 1992), whereas language skills do not appear to be related to test scores that appear to be relatively well defined as unique measures of verbal memory (e.g., percent retained or RI index; Hermann et al., 1988; Sass et al., 1992; Seidenberg et al., 1993). Of particular interest, Hermann et al. (1992a) found that naming score significantly predicted verbal memory performance in patients with right or left TLE. The relation between naming test performance and visual-spatial memory has not been assessed in the published literature.

In the next, and last, section of this review, the relationship between psychosocial factors and memory performance in persons with epilepsy is considered.

Psychosocial Factors

The relationship between psychosocial factors and memory performance

> *Psychosocial factors in epilepsy are as important, in my opinion, as any, with regard to the day-by-day functioning of the person with a seizure disorder.* (Dodrill, 1983, p. 341).

The term "psychosocial" is widely used and quite broadly defined. In the present context, it is used to refer to socially defined variables such as socio-economic status, level of education, occupational status, social stigma, and discrimination, as well as personally defined variables such as depression, anxiety, personality traits, and perceived quality of life. Of interest for the present study is the way in which such variables may be related to memory test performance in epilepsy patients (see Table 12). Psychosocial factors may influence performance on memory tests, or memory deficits may produce

psychosocial problems (Thompson, 1991). Alternatively, a third factor may underlie both psychosocial and memory difficulties. The correlational nature of studies in this area make it difficult to tease apart cause from effect.

Insert Table 12 about here

Previous research has shown that epilepsy is associated with increased incidence of many psychosocial problems. For example, the prevalence of depression and anxiety is raised in persons with epilepsy (Robertson, 1991). In Table 13 are listed some psychosocial problems that have been revealed by studies utilizing the Washington Psychosocial Seizure Inventory (WPSI), a self-report questionnaire designed specifically for use with persons with epilepsy. Also, patients often experience difficulties related to socio-economic status (SES). Thompson and Oxley (1988) found a substantial proportion of persons with epilepsy reported difficulties in work (71%), housing (29%), finance (37%), social activities (73%), relatives (28%), marriage/relationships (51%), and legal matters (3%).

Insert Table 13 about here

The relationship between psychosocial factors and cognitive performance is an issue that has been relatively neglected in the literature. This may be due to the inherent difficulty of teasing apart the likely subtle and interacting effects. Recent improvements in the way these factors are measured may help investigations in this area (e.g., Dodrill, 1983; Perrine et al., 1995). It is unfortunate that more research emphasis has not been placed on the role of psychosocial factors in memory and cognitive difficulties because

such factors may be more amenable to remediation than neurobiological factors (Thompson & Trimble, 1996).

Socio-economic status

Two studies have examined the effect of "cultural level" on memory function in persons with epilepsy. Loiseau et al. (1980) evaluated "a group where epilepsy is the sole symptom and the patients carry on relatively normal lives" (p. 61). They found that both professionals and students with epilepsy were poorer than matched controls on immediate figural recall, whereas manual workers with epilepsy performed as well as controls. Word list learning was poorer only for students with epilepsy when compared to controls, and word list recognition memory was poorer only for professionals with epilepsy in comparison with controls. It is remarkable that seizure type, seizure frequency, duration of epilepsy and anticonvulsant drugs had no effect in this study. Subsequent research by Loiseau et al. (1982) found that education level provided a significant unique contribution to the variance in total memory score according to multiple regression analysis. Furthermore, the only other significant factor was patient age; seizure type, EEG abnormality, duration of epilepsy, age at onset, seizure frequency, and anticonvulsant drug treatment all were not significant factors in the regression analysis. Taken together, these studies illustrate the importance of considering socio-economic status (SES) in experimental and control groups when evaluating memory function in persons with epilepsy. Also, these patients had relatively normal social adaptation. Perhaps the effect of SES would be less obvious in patients with more severe conditions.

MMPI / MMPI-2 scores

The MMPI is a widely used standardized questionnaire that yields 10 scales reflecting different personality, behaviour, and mood-related traits; particular patterns of high scale scores reflect particular personality types (Hathaway & McKinley, 1989).

Dodrill & Batzel (1986) found that MMPI average profile elevation was positively correlated with neuropsychological abnormality although the correlation accounted for only 3% of the common variance. They did not assess memory in particular. Stevens and colleagues (1972) found no difference between temporal lobe, generalized seizure, and frontal lobe groups on the MMPI or the WMS. They also found that patients who scored in the top one-third of each MMPI scale (indicating personality abnormality) did not tend to show more impaired neuropsychological test performance.

The depression scale of the MMPI tends to be the most elevated scale among persons with epilepsy (Hermann & Whitman, 1984). No published studies to date have attempted to relate MMPI-2 scores and memory test performance.

Quality of Life

A recent study by Perrine et al. (1995) investigated the relationship between psychosocial factors and memory functioning in more detail. A factor analysis including a neuropsychological test battery, the Profile of Mood States (POMS) inventory, and the Quality of Life in Epilepsy-89 (QOLIE-89) inventory[15] yielded 6 factors: Mood, Verbal Memory, Psychomotor, Visuospatial, Language, and Cognitive Inhibition. The tests that loaded on the Verbal Memory factor were word list learning and recall and immediate and delayed story recall. The test that loaded on the Visuospatial factor involved the copy, immediate recall, and delayed recall, of a complex figure. The Verbal Memory factor was correlated with the Attention/Concentration, Memory, and Health Discouragement QOLIE-89 scales. The Visuospatial factor was not correlated with any of the QOLIE-89 scales. A regression of the six factors on Overall QOLIE-89 score showed

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[15] The QOLIE-89 yields scores on the following scales: Health Perceptions, Seizure Worry, Physical Function, Role limits: Physical, Role limits: Emotional, Pain, Overall QOL, Emotional Well-being, Energy / Fatigue, Attention / Concentration, Memory, Language, Medication effects, Work / Driving / Social, Social Support, Social Isolation, Health Discouragement, and Overall QOLIE-89 score.

that Mood, Psychomotor Speed, Verbal Memory, and Cognitive Inhibition, in order of predictive strength, were significant predictors of overall quality of life. As the purpose of this study was to evaluate how neuropsychological test performance can predict self-reported quality of life, they did not attempt to predict memory test performance from quality of life or psychosocial factors. Nevertheless, the results suggested that verbal memory functioning played a relatively small but significant role in predicting quality of life. Whether quality of life also predicts or influences memory functioning remains to be evaluated.

Mood

The actual prevalence of mood disorders in epilepsy patients has not been conclusively established, but rates of depression and anxiety are higher in persons with epilepsy than the general population (Robertson, 1991). In addition, persons with epilepsy may have higher rates of depression than individuals with other chronic or neurological disorders. Mendez, Cummings, and Benson (1986) evaluated responses to behavioural, psychosocial, and disability questions given to persons with epilepsy and disabled persons without epilepsy. The two groups had "similar socioeconomic background", mean age, and gender ratio, and they were both "employable with training" (p. 766). The epilepsy group endorsed four items related to depression more frequently than the nonepilepsy group. However, there was no difference between the groups on questions related to anxiety. The authors concluded that "The frequency of interictal depression in community-based persons with epilepsy was greater ... than in a control population with similar socioeconomic and disability levels. This implies that the depression in epilepsy is more than a nonspecific reaction to a chronic disability" (p. 769).

Overall, the literature is inconsistent regarding the influence of depression on the existence, prevalence, nature, and specificity of neuropsychological deficits (Ercoli, Heaton, Peterkin, & Zisook, 1993). Depression has been associated with poor encoding, short term memory, learning, and retrieval on free recall tests, whereas recognition memory and automatic memory processes appear to be unaffected (Calev, Korin, Shapira, Kugelmass, & Lerer, 1986; Lezak, 1995). On the other hand, a detrimental effect of depression on memory performance is not always found (Ercoli et al., 1993; Grady & Seebauer, 1993). Perhaps results depend on the severity or type of depressive symptomatology in the research participants (Massmann, Delis, Butters, Dupont, & Gillin, 1992). When there is a detrimental effect, it may be that depression serves to lower motivation or to lower the amount of cognitive effort that can be exerted on the memory task. Low effort may be related to poor concentration, a less active learning strategy, or both (Baddeley, 1997; Hertel & Rude, 1991). In a related vein, it has been suggested that state anxiety can be related to poor verbal recall (Hill & Vandervoort, 1992). Anxiety can increase arousal level, which may have either a beneficial or a detrimental effect on memory, depending on the degree of arousal (Baddeley, 1997). Finally, both anxiety and depression may be related to worry and increased distactibility which, in turn, can affect test performance (Watts & Sharrock, 1985).

The relationship between mood and memory test performance in persons with epilepsy was examined by Corcoran and Thompson (1993). Patients who complained of memory problems performed more poorly on immediate and delayed story recall and design learning, but there were no differences between the groups on the remaining neuropsychological tests (see Table 12). Further analyses revealed that complainers were more likely to use mnemonic strategies and were more depressed and anxious than non-complainers. In addition, depression was significantly associated with poor immediate

story recall and design learning, and anxiety was significantly associated with poor immedate and delayed story recall and design learning. This study did not provide information regarding why or how mood disturbance was related to memory. For example, experiencing memory problems may induce symptoms of depression and anxiety, or depresson or anxiety may produce poor performance on memory tests. Furthermore, a third variable, such as seizure onset in the temporal lobe, or long duration of epilepsy, could produce both mood and memory difficulties. Indeed, the complainers had a significantly older age at onset of seizures (mean onset at 20 years of age) than non-complainers (mean onset at 14 years of age) and complainers with older seizure onset had a higher incidence of symptoms of mood disturbance. A more sophisticated research design would be necessary to make progress toward understanding the interaction between these variables.

Dodrill's (1986) findings suggested that mood was not solely responsible for the cognitive deficits of patients with generalized seizures. Patients with the highest lifetime number of seizures obtained lower scores on measures of mood and psychosocial functioning, but patients with a history of status epilepticus obtained the lowest IQ and neuropsychological test scores.

Gender

Most previous studies have found no significant relationship between gender and memory functioning in epilepsy patients (Hermann et al., 1988; Làdavas et al., 1979; Rausch et al., 1978; Seidenberg et al., 1993). The study by Strauss et al. (1992), described earlier, investigated the influence of patient gender and development of atypical speech dominance on memory performance in a group of patients in whom seizure onset occurred before one year of age. This study employed rather small group sizes but it provided tentative evidence that very early onset of epilepsy and patient gender

interacted, such that males with left hemisphere dysfunction before one year of age suffered generalized cognitive deficits, whereas females with left hemisphere dysfunction with onset before their first birthday displayed deficits that were related to a shift in speech localization.

One study found an effect of gender on memory functioning in TLE patients (McGlone, 1994). Significant effects on delayed verbal recall were found for both gender and side of epileptogenic focus; females outperformed males, and patients with a RTL focus outperformed patients with a LTL focus. However, with regard to visual-spatial recall performance, there was an interaction between side of temporal lobe focus and gender. Males with a left temporal focus outperformed males with a right temporal focus as well as females with a left temporal focus. Thus, patient gender appeared to mediate the effect of unilateral temporal lobe focus on visual-spatial memory performance.

Summary

Persons with epilepsy are subject to particular social stressors and display increased rates of particular emotional symptoms (Levin, Banks, & Berg, 1988; Robertson, 1991; Thompson & Oxley, 1988). Studies in France indicate that memory test performance varies according to SES in relatively well-adapted persons with epilepsy (Loiseau et al., 1980; 1982). No relationship between high MMPI scale scores (i.e., personality disturbance) and memory has been found (Stevens et al., 1972). The relationship between the personality traits measured by the MMPI-2 and memory test performance has not been investigated. Verbal memory performance appears to help predict self-reported quality of life (Perrine et al., 1995), but it is not known how measures of quality of life might predict memory performance. Patient gender may influence memory outcome when age at onset is prior to one year of age (Strauss et al., 1992) and gender may mediate the effect of side of temporal lobe epileptogenic focus

such that only males evidence a negative effect of RTL focus on visual-spatial memory (McGlone, 1994). Depression and anxiety levels appear to be negatively related to memory test performance in persons with epilepsy (Corcoran & Thompson, 1993). The impact of these variables on memory in person with chronic TLE, in particular, has not been evaluated.

Summary and Hypotheses

Studies that have compared the memory test scores of persons with epilepsy to normal controls have consistently found the patients' scores to be significantly poorer (e.g., Loiseau et al., 1983; Randolph et al., 1994), especially vis-à-vis measures of delayed memory (Breier et al., 1996; Delaney et al., 1980; Giovagnoli & Avanzini, 1996; Jones-Gotman, 1991). Initial attempts to understand the factors that might underlie memory deficits in these patients examined seizure-related variables such as age at seizure onset, duration of epilepsy, seizure frequency, seizure type, and etiology. In general, the results of these investigations were disappointing (e.g., Delaney et al., 1980; Hermann et al., 1988; Loiseau et al., 1980; Rausch et al., 1978; Scott et al., 1967). Among seizure-related variables, only duration of epilepsy appears to have a significant negative relationship with memory performance (Delaney et al., 1980; Làdavas et al., 1979; Loiseau et al., 1982; Mirsky et al., 1960), although this relationship has not been found invariably (Hermann et al., 1988; Loiseau et al., 1980; 1983; Rausch et al., 1978; Scott et al., 1967).

In the wake of results indicating material-specific memory deficits in post-surgical epilepsy patients with unilateral temporal lobe lesions (Milner, 1971), research began to focus on the relationship between temporal lobe seizure focus and memory test performance. The research evidence indicates that a left temporal lobe seizure focus is related to verbal memory deficits, and a right temporal lobe focus is related to visual-spatial memory deficits (Breier et al., 1996; Delaney et al., 1980; Làdavas et al., 1979; cf. Mayeux et al., 1980). These effects are more likely to be found when comparing each temporal lobe group to a control group, rather than when comparing the temporal lobe groups to each other (e.g., compare Breier et al. (1996) to Thompson and Trimble

(1996)). That is, both temporal lobe groups show memory difficulties, and more pronounced material-specific deficits may be present according to side of focus.

Only one study specifically investigated the effect of duration on verbal and visual-spatial memory in left versus right temporal lobe patient groups (Làdavas et al., 1979). Patients who had a duration of epilepsy of greater than one year obtained a greater discrepancy between their verbal and visual-spatial learning and delayed recall scores than those having a duration of less than one year. These findings suggested that longer duration is associated with a greater relative decrement in verbal memory in persons with left temporal lobe epilepsy and a greater relative decrement in visual-spatial memory in persons with right temporal lobe epilepsy. Hence, it is possible that other important factors accentuate the decrement in verbal and visual-spatial memory often shown by LTL and RTL groups, respectively. Such an interaction might help explain why the effect of unilateral temporal lobe focus on material-specific memory is not always found.

Hippocampal pathology in the left hemisphere is also related to verbal memory deficits (Baxendale et al., 1998; Kälviäinen et al., 1997; Lencz et al., 1992; Miller et al., 1993; Rausch & Babb, 1993; Saling et al., 1993; Sass et al., 1990; 1992; 1995). In contrast, right hemisphere hippocampal pathology does not appear to be related to visual-spatial memory deficits, according to traditional measures (Baxendale et al., 1998; Lencz et al., 1992; McMillan et al., 1987; Miller et al., 1993; Rausch & Babb, 1993).

In most cases, memory deficits in persons with epilepsy are not related to structural brain lesions. The electrical activity of the seizure focus appears to be more important with respect to memory functioning than cerebral pathology (other than hippocampal sclerosis; Làdavas et al., 1979; Sass et al., 1995). Anticonvulsant drugs may affect attention, concentration, and motor speed (Dodrill & Temkin, 1989; Duncan et al., 1990; Trimble & Thompson, 1983), but there is little objective evidence to suggest

that anticonvulsants have a detrimental effect on memory processes per se (Delaney et al., 1980; Homan et al., 1989; Loiseau et al., 1980; 1982; 1983; Rausch et al., 1978; Verhoeff et al., 1992).

In addition to neurobiological factors, other cognitive factors may be related to memory performance (Christianson, 1994; Thompson, 1991). For example, in order to perform at an optimal level on a memory test, a number of cognitive functions are required such as basic perception and response capability, attention, and language skills. However, previous research has failed to show a significant relationship between memory test scores and cognitive variables such as FSIQ (Dodrill, 1986; Loiseau et al., 1984; Sass et al., 1995; Schwartz & Dennerll, 1969; Seidenberg et al., 1993; Thompson & Trimble, 1996; cf. Mirsky et al., 1960), attention and concentration skills (Dodrill, 1986; Helmstaedter et al., 1991; Loiseau et al., 1984), and Verbal IQ (Hermann et al., 1988; Rausch & Babb, 1993; Sass et al., 1990; cf. Sass et al., 1992) in persons with epilepsy, especially when memory deficits are present. On the other hand, preliminary evidence suggests that persons with epilepsy display poorer metamemory and use of strategy than control subjects (Powell et al., 1984; Prevey et al., 1988; 1991; Seidenberg et al., 1993), although it has not been determined whether these shortcomings appreciably affect memory test performance. The possible relationship between visual-spatial skills and memory performance in epilepsy patients remains to be investigated. The most compelling finding in this area is that object naming performance is positively related to verbal memory test performance in persons with epilepsy (Hermann et al., 1988, 1992a; Mayeux et al., 1980; Sass et al., 1992). A relationship between naming and visual-spatial memory has not been investigated in the epilepsy literature.

It has been suggested that the association between poor verbal memory and poor naming performances may reflect a general inefficiency in retrieving stored information

(Hermann et al., 1988). However, research by Seidenberg et al. (1993) found that the recognition memory errors displayed by LTL patients suggest that their verbal memory deficits are at least partially independent of a general retrieval problem.

Finally, psychosocial factors may be related to memory performance. Persons with epilepsy are subject to particular social stressors and display increased rates of particular emotional symptoms, including depression and anxiety (Levin et al., 1988; Mendez et al., 1986; Robertson, 1991; Thompson & Oxley, 1988). Overall, the amount of research investigating the psychosocial correlates of memory dysfunction in persons with epilepsy is meager. However, research by Corcoran and Thompson (1993) suggests that depression is associated with poor immediate story recall and design learning, and anxiety is associated with poor immediate and delayed story recall and design learning, in a heterogeneous sample of persons with epilepsy. In addition, patients who complained of memory problems had a relatively older age at onset of seizures (i.e., shorter duration) as well as a higher level of mood disturbance. There is no evidence to suggest that overall MMPI score influences memory performance (Stevens et al., 1972) and the relationship between other psychosocial factors and memory functioning in these patients requires more research.

Hypotheses

The purpose of the present research was to apply a multifactorial approach to the investigation of factors related to memory problems in persons with epilepsy, and to delineate the most important factor or set of factors with respect to memory outcome. A review of the literature in three domains – neurobiological, cognitive, and psychosocial – revealed a reduced number of factors that appear to be important. Previous research has focused primarily on the relationship between side of temporal lobe seizure focus and specific memory deficits, although duration of epilepsy, object naming performance, and

levels of depression and anxiety also appear to be important. Hence, the relationship between these five variables and memory functioning in the verbal and visual-spatial domains was investigated in this study. Based on the above review, the following hypotheses were formulated:

1. Epilepsy patients' memory test scores will be lower than those of the standardization samples. Specifically, these differences are expected on measures of delayed memory rather than measures of immediate memory.

2. Memory tests requiring the recollection of words or stories will be related to an underlying "verbal" memory component, and memory tests requiring the recollection of figures will be related to an underlying visual-spatial memory component.

3. Duration of epilepsy, BNT score, level of depression, and level of anxiety will each account for a significant proportion of the variance in the memory component scores of the epilepsy patients.

4. Patients with a LTL seizure focus will obtain relatively poor verbal memory component scores, whereas patients with a RTL seizure focus will obtain relatively poor visual-spatial memory component scores.

5. Duration, naming, depression, and anxiety will each accentuate the decrement in verbal and visual-spatial memory shown by the left and right temporal lobe groups, respectively (as described in hypothesis 3).

CHAPTER III

Method

Participants

The records of a consecutive sample of patients with epilepsy who completed a neuropsychological assessment between April 1993 and January 1998, at the Henry Ford Health Center, Detroit, Michigan, were scrutinized. One hundred forty-two patients met the following criteria: 18 years of age or older, prorated Full Scale IQ score greater than 69, and no history of previous neurosurgery. Most participants completed a comprehensive evaluation for the Epilepsy Surgery Program that included: neuropsychological assessment, baseline EEG, prolonged video-EEG, intracarotid sodium amytal test, Magnetic Resonance Imaging (MRI) scan, and interictal Single Photon Emission Computed Tomography (SPECT).

The patients were classified into five groups according to suspected site of seizure focus: left temporal lobe (LTL), right temporal lobe (RTL), both temporal lobes (BTL), non-temporal or undetermined focus[16] (NT/U), and patients who were not surgery candidates (NS)[17]. The decision regarding site of seizure focus was made via consensus of the clinicians involved with the various aspects of the presurgical evaluation.

Demographic, neurobiological, and neuropsychological characteristics of this sample are described in Table 14, grouped according to patient group. There were no significant differences among the patient groups on these continuous variables (oneway ANOVA or Kruskal-Wallis H test, all ps > .05), with the exception of RAVLT Discriminability score ($\chi^2 = 15.4$, $p = .004$). Post hoc comparisons, with a family wise

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[16] For 11 patients no seizure focus could be determined. One patient had a frontal lobe seizure focus and one patient had an "extra-temporal" lobe seizure focus.

[17] Ten patients had been referred for neuropsychological assessment because of complaints of memory problems or other cognitive difficulties and six did not complete the comprehensive evaluation.

error rate of $\alpha = .01$, indicated that the BTL group scored significantly lower than the RTL group (Mann-Whitney U test: $z = -3.09$, $p = .002$) and the NS group ($z = -2.67$, $p = .008$) on this measure.

Insert Table 14 about here

The frequencies of the categorical variables are represented in Table 14 as the percentage of participants in one level of each variable, for each group. There were no significant differences among the patient groups on the categorical variables (χ^2 test, all $ps > .05$) with the exception of the use of subdural electrodes to help detect location of seizure focus. Patients in the LTL and RTL groups were both more likely to have undergone subsequent neurosurgery than the BTL ($z = -3.64$, $p < .001$ and $z = -4.38$, $p < .001$, respectively) or NT/U ($z = -4.65$, $p < .001$ and $z = 5.38$, $p < .001$, respectively) groups. None of the patients in the NS group later underwent neurosurgery. These results indicate that patients whose video EEG showed evidence of bitemporal foci or no evidence of a specific focus were less likely to undergo surgical intervention.

Materials and Procedure

Data for each patient were collected from his or her hospital records. The variables included in the present study were as follows:

Independent variables

1. Location of seizure focus: In most cases determined via subdural electrode monitoring or site of actual neurosurgical intervention. In a minority of cases determined via 24 hour EEG monitoring.

2. Duration of epilepsy: Obtained from patient records and reported in years.

3. Boston Naming Test (BNT): Standardized test of object naming. Participants are asked to name up to 60 line drawings (Kaplan, Goodglass, & Weintraub, 1983).

4. MMPI-2 Clinical Scale 2 (Scale 2; Depression): Higher scores indicate increased symptoms of depression (Butcher & Williams, 1992).

5. MMPI-2 Clinical Scale 7 (Scale 7; Psychasthenia): Higher scores indicate increased symptoms of anxiety (Butcher & Williams, 1992).

Dependent variables (memory tests)

1. Wechsler Memory Scale - Revised (WMS-R; Wechsler, 1987), Logical Memory I (LMI) subtest: Two short stories (one paragraph long each) are read to the participant. The participant recalls each story immediately after presentation.

2. WMS-R, Logical Memory II (LMII) subtest: After a 30 minute delay, the participant again recalls each story that was presented in the LMI subtest.

3. Rey Auditory Verbal Learning Test, Long Delay recall trial (RAVLT-LD): First, a list of 15 words is read to the participant over five learning trials. Second, an intervening word list is read and recalled once. Third, the participant is asked to recall the initial word list (Short Delay recall trial). Twenty minutes later the Long Delay recall trial occurs when the participant is instructed to recall as many words from the initial word list as possible.

4. RAVLT Retroactive Interference Index (RAVLT-RI): A measure of retroactive interference due to the intervening word list of the RAVLT. It is calculated as: (RAVLT short delay recall / RAVLT trial 5) x 100.

5. RAVLT Discriminability (RAVLT-Discrim): A measure of ability to discriminate between words from the RAVLT word list and new words during a recognition memory test. It is calculated as: (1 - ((false positives + misses) / 50)) x 100.

6. WMS-R, Visual Reproduction I (VRI) subtest: Four figures (single line drawings) are presented for 10 seconds, each on a separate trial. The participant reproduces each figure immediately after presentation.

7. WMS-R, Visual Reproduction II (VRII) subtest: After a 30 minute delay, the participant again reproduces each figure that was presented in the VRI subtest.

8. Rey-Osterreith Complex Figure Test Delayed Recall (ROCFT-D): The participant copies a complex figure and then attempts to reproduce it immediately afterward. After a 30 minute delay, the Delayed Recall trial occurs when the participant again attempts to reproduce the complex figure.

9. Recurring Figures Discriminability (RF-Discrim): A measure of ability to discriminate between previously presented abstract figures (Kimura, 1963) and new abstract figures during a recognition memory test. It is calculated as: (1 - ((false positives + misses) / 70)) x 100.

Note: For comparison with standardization samples, the memory test scores were transformed into standardized T scores based on published means and standard deviations, where possible. Standardization data for the Logical Memory and Visual Reproduction subtests were provided in the WMS-R manual[18] (Wechsler, 1987). Data for RAVLT-LD were provided by Geffen, Hoar, O'Hanlon, Clark, and Geffen (1990) and data for the ROCFT-D were provided by the Rey Complex Figure Test and Recognition Trial Manual (Meyers & Meyers, 1995). These transformations indicated deviation from the standardized mean while taking the effect of age into consideration.

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[18] The WMS-R manual provides normative means and standard deviations for the following age groups: 16-17, 20-24, 35-44, 55-65, 65-69, 70-74. Means and standard deviations were estimated for the 18-19, 25-34, 45-54 age groups using data from the immediately pre and post age groups. The necessary statistics were calculated (i.e., Σy^2, Σy, total n) for the pre and post age groups, and the data were combined.

Statistical Analyses

The following statistical analyses were used to evaluate each hypothesis.

Hypothesis 1: T-tests were used to compare the mean T scores of the epilepsy patients to the mean scores of standardization samples (i.e., T score of 50) on each memory test for which standardization data were available. Also, z tests of independent proportions were used to compare the proportion of patients scoring in the impaired range to that of standardization samples.

Hypothesis 2: A Principal Components Analysis (PCA) was conducted to determine whether four measures of delayed verbal memory were all related to an underlying "verbal" memory component and three measures of delayed visual-spatial memory were all related to an underlying "visual-spatial" memory component, as well as to create new verbal memory and visual-spatial memory component scores.

Hypothesis 3: Two multiple regression analyses were conducted with (1) verbal component score and (2) visual-spatial component score as dependent variables. Each multiple regression contained six predictor variables: four factors of interest (i.e., duration of epilepsy, BNT score, level of depression, and level of anxiety) plus age and education.

Hypothesis 4: Two separate oneway ANOVAs were conducted to assess differences between the LTL and RTL groups on (1) verbal memory component score and (2) visual-spatial memory component score.

Hypothesis 5: A series of analyses were conducted to test whether each predictor variable interacted with side of temporal lobe seizure focus in relation to (1) verbal memory component and (2) visual-spatial memory component. Each hierarchical multiple regression analysis tested, in order, (1) the main effect of unilateral TL focus, (2) the main effect of each predictor variable, and (3) the interaction between these two variables (i.e., after accounting for the main effects) on memory component score.

CHAPTER IV

Results

Data screening

An outlier was found in the distribution of VRI raw scores ($z = 3.90$, $p < .001$). The case was a 41 year old female with a left temporal lobe seizure focus and a five year duration of epilepsy. The score was changed from 7 to one unit smaller than the next most extreme score in the distribution (i.e., 13; Tabachnick & Fidell, 1996). Also, an outlier in the distribution of RI index scores was found. The patient, who had a score of zero, was a 37 year old female with a duration of epilepsy of 14.5 years and she was not a surgery candidate. The RI index score was changed to one unit smaller than the next most extreme score in the distribution (i.e., 19).

The distributions of BNT, RAVLT-Discrim, RI index, and VRI were significantly negatively skewed (see Table 14 footnote). Transformation of these variables was undesirable because it would have changed the scale of the scores.[19] Examination of residuals scatterplots (i.e., histogram of standardized residuals, normal probability plot of standardized residuals, and scatterplot of standardized predicted values and standardized residuals) indicated that assumptions for normality were met. Therefore, the variables were entered without violating the assumptions of multivariate analysis. No multivariate outliers were detected among the patients, with $p = .001$. Assumptions regarding normality of sampling distributions, homogeneity of variance-covariance matrices, linearity, and multicollinearity were met for all of the following analyses.

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[19] Also, attempts to normalize the distribution of RAVLT Discrim -- utilizing reflect and square root, reflect and log, and reflect and inverse transformations -- were all unsuccessful.

Epilepsy patients versus standardization samples

To simplify comparison of patients with the standardization sample of each memory test, a standardized T score was calculated for each patient, according to age group, for the six measures of delayed memory for which normative data were available: T-LMI, T-LMII, T-RAVLT-LD, T-VRI, T-VRII, and T-ROCFT-D. The mean T scores of the epilepsy patients on each memory measure are represented in Figure 1. Each mean T score was compared to the standardized mean of 50 using one sample t-tests. To control for increased risk of a type I error due to multiple comparisons, an α level of .01 was used for each test (Tabachnik & Fidell, 1996). The results indicated that the patients scored significantly lower than the standardized mean of 50 on five of the six memory tests: T-LMI (t (141) = -5.80, $p < .001$), T-LMII (t (141) = -8.13, $p < .001$), T-RAVLT-LD (t (133) = -8.45, $p < .001$), T-VRII (t (140) = -7.93, $p < .001$), and T-ROCFT-Delay (t (139) = -11.83, $p < .001$). T-VRI was marginally different from 50 (t (141) = -1.81, $p <$ .05, one-tailed).[20] The strength of association between group membership (epilepsy group or standardization sample) and each memory test score (η^2) indicated that the total variances in T-LMI, T-LMII, T-RAVLT-LD, T-VRI, T-VRII, and T-ROCFT-D that were predictable from group membership were 4.8%, 8.5%, 17.2%, 0.6%, 13.3%, and 28.0%, respectively. Therefore, while the groups differed significantly on memory test performances, variables other than group membership (and age) appeared to account for the majority of the variance in memory test performance.

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[20] The distribution of T-VRI was negatively skewed (skewness = -1.026, z = -5.054, $p < .001$). However, given that the sample size was large (n=142) and that transforming the distribution would have yielded meaningless scores, the distribution was not changed. Also, the median of T-VRI was 50.19.

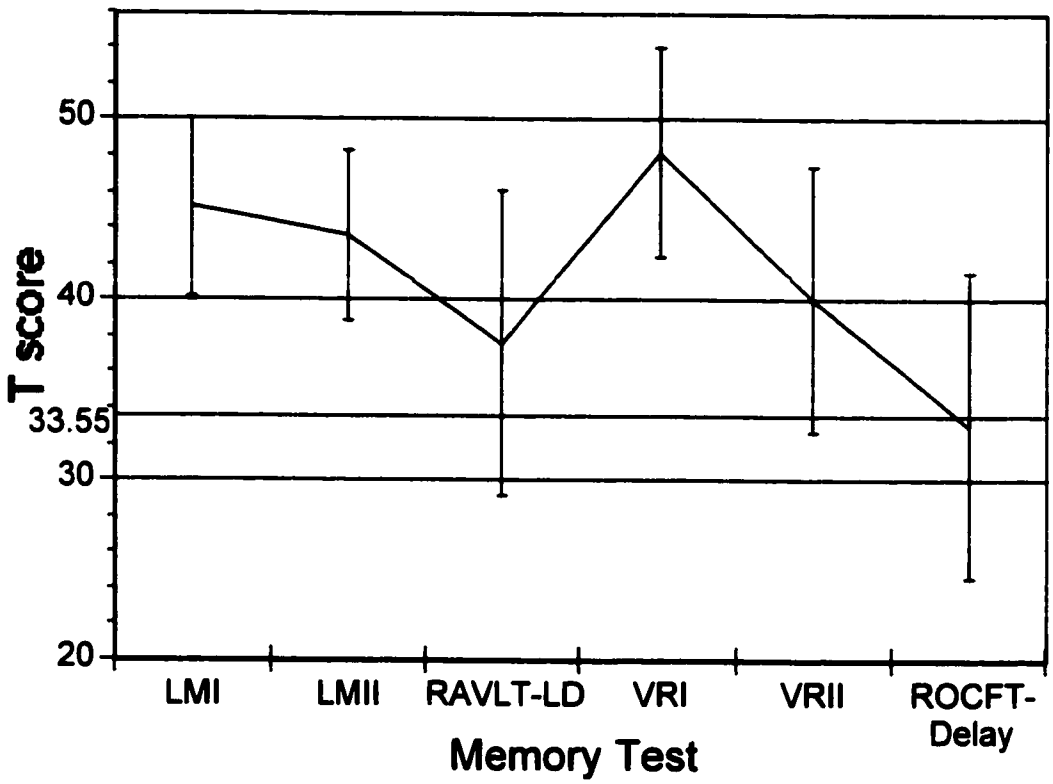

Figure 1. Mean T scores for persons with epilepsy on six memory measures. Error bars represent one standard deviation above and below each mean.

A second set of analyses was conducted to determine whether a larger than expected proportion of patients obtained a memory test score in the impaired range. A score lower than the 5th percentile of the standardization sample (i.e., a T score less than 33.55) was considered to be in the impaired range (see Table 15). Z tests of independent proportions indicated that the proportion of epilepsy patients who scored in the impaired range on each memory test was significantly greater than .05 on five of the memory tests: T-LMI ($z = -3.27$, $p < .001$), T-LMII ($z = -3.86$, $p < .001$), T-RAVLT-LD ($z = -6.95$, $p < .001$), T-VRII ($z = -6.35$, $p < .001$) and T-ROCFT-Delay ($z = -9.47$, $p < .001$). The observed z value for T-VRI fell just at the statistically significant level ($z = -2.31$, $p = .01$, one-tailed).

Insert Table 15 about here

Reducing variables to verbal memory and visual-spatial memory components

A PCA was conducted to determine whether four measures of delayed verbal memory were all related to an underlying "verbal" memory component and three measures of delayed visual-spatial memory were all related to an underlying "visual-spatial" memory component, as well as to create new verbal memory and visual-spatial memory component scores. The four "verbal" tests included two measures of delayed recall (LMII and RAVLT-LD), one measure of discriminability (RAVLT-Discrim), and one measure of retroactive interference (RAVLT-RI). The three "visual-spatial" tests included two measures of delayed recall (VRII and ROCFT-D) and one measure of discriminability RF-Discrim).

PCA with varimax rotation was performed on the seven memory measures for the 142 patients. There were a small number of missing values; eight patients did not

complete the RAVLT because a different word list learning test had been introduced to the neuropsychological test battery. The missing values were substituted with the variable mean (Tabachnick & Fidell, 1996). Two components were extracted. As expected, the four verbal memory measures loaded on the first component, and the three visual-spatial memory measures loaded on the second component (see Table 16). Therefore, the first component score was used to represent verbal memory, and the second component score was used to represent visual-spatial memory in subsequent analyses.

Insert Table 16 about here

The distributions of the verbal and visual-spatial memory components formed normal z distributions with means of zero and standard deviations of one. To ease interpretation of these scores, they were transformed to T scores by multiplying by 10 and adding 50 to each score. The descriptive statistics of the verbal and visual-spatial memory T scores, by patient group, are presented in Table 17.

Insert Table 17 about here

Memory component score prediction

It was hypothesized that duration of epilepsy, BNT score, level of depression, and level of anxiety would predict memory performance.[21] Also, because age and education[22] are related to selected variables (see Table 18), and they are often related to

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[21] Patient group could not be included as a predictor variable in these analyses secondary to inadequate sample size.

[22] Education was recoded into two categories: _12 years or >12 years.

memory test performance, they were also included as predictor variables. Two multiple regression analyses were conducted with (1) verbal component score and (2) visual-spatial component score as dependent variables. Table 18 displays the correlations among the predictor variables, the verbal memory component, and the visual-spatial memory component.

Insert Table 18 about here

Verbal memory

To determine the unique predictability of each variable on the verbal memory component, a simultaneous multiple regression analysis was conducted (see Table 19). Taken together, the six predictor variables predicted 7.0% of the variance in the verbal memory component. However, the proportion of variance accounted for was not significant ($F(6,105) = 1.32$, $p = .25$). The only variable that was a significant unique predictor of verbal memory was BNT. It uniquely predicted 5.0% of the variance in verbal memory. Holding all other predictor variables constant, as scores on the BNT increased, scores on the verbal memory component also increased ($\beta = .23$, $p < .02$). Moreover, BNT was the only predictor variable that was significantly correlated with verbal memory.

Insert Table 19 about here

Visual-spatial memory

To determine the unique predictability of each variable on the visual-spatial memory component, a simultaneous multiple regression analysis was conducted (see

Table 20). Taken together, the six predictor variables accounted for 23.7% of the variance in the visual-spatial memory component. The proportion of variance accounted for was significant ($F(6,105) = 5.43$, $p < .001$). BNT, Scale 7, and age were significant unique predictors of visual-spatial memory. They uniquely predicted 9.5%, 3.1%, and 3.7% of the variance in visual-spatial memory, respectively. Holding all other predictor variables constant, as scores on the BNT increased, scores on the visual-spatial memory component increased ($\beta = .32$, $p < .001$). Conversely, holding all other predictor variables constant, as scores on Scale 7 increased, scores on the visual-spatial memory component decreased ($\beta = -.26$, $p < .05$). Similarly, as age increased, scores on the visual-spatial memory component decreased ($\beta = -.23$, $p < .03$). Five out of six predictor variables were significantly correlated with visual-spatial memory. Apparently the relationships between Scale 2 and duration, and visual-spatial memory, were mediated by, or redundant with, the relationships between BNT, Scale 7, and age, and visual-spatial memory.

Insert Table 20 about here

Missing data and generalizability

Twenty-eight of the 142 patients had missing MMPI-2 data. These cases were examined to investigate whether they differed from the remaining cases on any variables. Statistical comparisons indicated that patients with missing MMPI-2 data did not differ from patients with MMPI-2 data on duration, patient group, age, education, gender, or verbal memory component (all $ps > .10$). However, the patients with missing MMPI-2 data scored significantly lower on the BNT (MMPI-2 missing: median = 40; MMPI-2 not missing: median = 50; Mann-Whitney $z = -3.00$, $p = .003$), the visual-spatial memory

component (MMPI-2 missing: mean = 43.61, SD=10.94; MMPI-2 not missing: mean = 51.57, SD = 9.14; $t(140) = 3.96$, $p < .001$), and Full Scale IQ (MMPI-2 missing: mean = 85.6, SD = 15.1; MMPI-2 not missing: mean = 94.3, SD = 11.7; $t(140) = 3.33$, $p = .001$). Therefore, caution should be exercised in generalizing these results to patients with very low BNT, visual-spatial memory, or Full Scale IQ scores.

The effect of seizure focus on verbal and visual-spatial memory

Two separate oneway ANOVAs were conducted to assess differences between the LTL and RTL groups on (1) verbal memory component score and (2) visual-spatial memory component score. With the verbal memory component as the dependent variable, the effect of seizure focus group was statistically significant ($F(1,94) = 9.95$, $p < .003$). The LTL group obtained a significantly lower verbal memory component score than the RTL group (see Table 17). The strength of association (η^2) indicated that 9.6% of the variance in the verbal memory component was attributable to seizure focus group.

With the visual-spatial memory component as the dependent variable, the effect of patient group was not significant ($F(1,94) = 1.95$, $p = .17$). There was no significant difference between the LTL and RTL groups on the visual-spatial memory component score, although the trend was in the expected direction (see Figure 2).

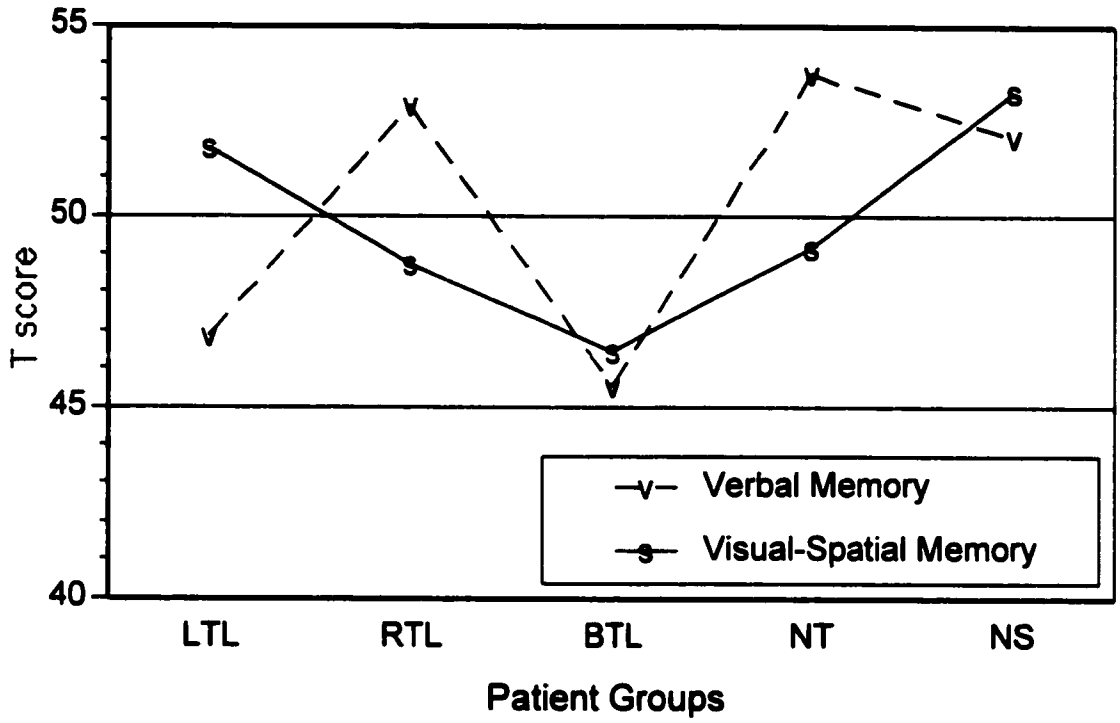

Figure 2. Verbal and visual-spatial memory component scores for each patient group. The patient groups that displayed evidence of a LTL seizure focus (i.e., LTL and BTL) obtained verbal memory scores below the mean of 50, whereas the groups that displayed no evidence of a LTL seizure focus (i.e., RTL and NT/U) obtained verbal memory scores above the mean of 50. Also, the RTL and NT/U groups obtained virtually identical verbal and visual-spatial memory test scores. Only the LTL and NS groups obtained a mean visual-spatial memory score above 50.

The interaction between side of TL seizure focus and pattern of memory component scores was analyzed by comparing patient groups on (1) the number of patients whose verbal component score was 5 points (half a standard deviation) higher than their visual-spatial component score, (2) the number of patients whose visual-spatial component score was 5 points higher than their verbal component score, and (3) the number of patients whose verbal and visual-spatial component scores were within 5 points of each other (see Table 21). The RTL group was significantly more likely to have verbal score higher than visual-spatial score, and the LTL group was significantly more likely to have visual-spatial score higher than verbal score (χ^2 (1) = 8.56, $p < .01$). Also, the BTL group appeared to be more likely to obtain similar verbal and visual-spatial component scores (χ^2 (4) = 14.45, $p < .01$).

Insert Table 21 about here

The above analyses included some patients with atypical left hemisphere speech dominance (see Table 14). In order to avoid any possible confounds resulting from including these patients, the results were run again with only patients with documented left hemisphere speech dominance included. For each analysis the results were equivalent. With the verbal memory component as the dependent variable, the effect of seizure focus group was statistically significant ($F(1,51) = 10.76$, $p < .002$), and with the visual-spatial memory component as the dependent variable, the effect of patient group was not significant ($F(1,51) = 0.10$, $p = .74$). Also, the RTL group was significantly more likely to have verbal score higher than visual-spatial score, and the LTL group was significantly more likely to have visual-spatial score higher than verbal score (χ^2 (1) =

4.10, $p < .05$; see Table 22). Again, the BTL group appeared to be more likely to obtain similar verbal and visual-spatial component scores (χ^2 (4) = 14.16, $p < .01$).

Insert Table 22 about here

Patients tested as inpatients versus patients tested as outpatients

To examine whether the patients who were tested as inpatients (i.e., undergoing video EEG with reduced anticonvulsant levels) displayed the same results as those tested as outpatients (i.e., with anticonvulsant levels as prescribed by physician), an ANOVA was conducted in which side of temporal lobe focus and testing location served as independent variables, and memory component served as the dependent variable. The intention of this analysis was to rule out an interaction between side of temporal lobe focus and testing location on each memory component. The result for the verbal memory component showed a main effect for side of focus ($F(1,92) = 10.12$, $p = .002$) but no main effect for testing location and no effect for the interaction (ps _ .09). For the visual-spatial memory component, the main effects and interaction were all nonsignificant (all ps > .10). Therefore, there is no evidence that patients who were tested as inpatients obtained a significantly different pattern of verbal and visual-spatial memory component scores in relation to RTL and LTL focus than those who were tested as outpatients.

Interactions between side of temporal lobe focus and each predictor variable

In this section, the relationship between unilateral temporal lobe seizure focus and material-specific memory functioning was examined in more detail. In particular, the hypothesis that each significant predictor variable would interact with side of temporal lobe focus to accentuate the difference between the RTL and LTL groups on memory performance, was tested. A series of hierarchical multiple regression analyses was used

to test, in order, (1) the main effect of unilateral TL focus, (2) the main effect of each predictor variable, and (3) the interaction between the first two variables (i.e., after accounting for the main effects) on the verbal memory and visual-spatial memory component scores (Cohen & Cohen, 1983; Fong, personal communication). To control for experimentwise error rate, $\alpha = .01$ was used (Tabachnik & Fidell, 1996).

The results failed to show a significant interaction between any of the predictor variables and unilateral temporal lobe seizure focus (see Table 23) with regard to the two memory component scores. There was one marginal interaction between depression (Scale 2) and unilateral focus (F Change = 4.10, $p < .05$) with verbal memory as the dependent variable, however, depression appears to have acted as a suppressor variable in this analysis. The correlation between verbal memory and depression was near zero ($r = .06$), whereas the correlation between verbal memory and the product of depression and unilateral focus was significant ($r = .30$, $p < .01$) and the correlation between depression and the product of depression and side of focus was significant ($r = .28$, $p < .02$). Given that depression shared no appreciable variance with verbal memory but depression was correlated with the product of depression and side of focus, depression likely served to suppress irrelevant variance between the product of depression and side of focus and verbal memory (Pedhazur, 1982). Therefore, the marginal interaction between depression and side of temporal lobe seizure focus with respect to verbal memory is considered to be spurious.

Insert Table 23 about here

According to the results presented in Table 23, none of the four predictor variables contributed to the prediction of verbal memory component after the effect of

side of temporal lobe focus had been taken into account. In addition, none of the four predictor variables were significantly correlated with the verbal memory component when considering only the unilateral temporal lobe patients. Thus, the significant correlation between BNT and verbal memory component, evident with the entire epilepsy sample, was not obtained with the subsample of unilateral TL patients.

In contrast, BNT and duration significantly, and anxiety marginally, contributed to the prediction of visual-spatial memory component after the effect of side of temporal lobe focus had been taken into account. However, given the logical link between age and duration, and the finding that age was a significant predictor of visual-spatial memory component within the entire epilepsy sample (see Table 20), it seemed prudent to examine whether the relationship between duration and visual-spatial memory was mediated by age. When considering only the unilateral TL patients, the correlation between age and visual-spatial memory performance was nonsignificant ($r = -.17$, $p = .09$; compare with the significant result when considering the entire epilepsy sample shown in Table 18). Also, a multiple regression analysis with the visual-spatial memory component as the dependent variable, and side of focus, age, and duration as predictor variables indicated that the effect for duration was marginally significant when age was included as a predictor ($\beta = -.25$, $p < .03$) and neither age nor side of focus was significant ($\beta = -.06$, $p = .56$, and $\beta = .18$, $p = .08$, respectively). Thus, duration, but not age, appears to be a marginally significant unique predictor of visual-spatial memory component when considering only the unilateral TL patients (see Table 24). Conversely, age, but not duration, appears to be a significant unique predictor of visual-spatial memory when considering the entire epilepsy sample (see Table 25).

Insert Table 24 about here

Insert Table 25 about here

CHAPTER V

Discussion

The present study was undertaken to investigate factors that may be associated with poor memory functioning in persons with epilepsy. Based on a review of related literature, five factors were determined to be the most likely correlates of memory problems. These factors were side of TL seizure focus, duration of epilepsy, BNT score, anxiety, and depression. Five hypotheses regarding the relationship between these factors and memory performance were formulated and tested. The ability or failure to support each hypothesis is discussed below, followed by a discussion of issues raised by the results.

Hypothesis 1

> *Epilepsy patients' memory test scores will be lower than those of the standardization samples. Specifically, these differences are expected on measures of delayed memory rather than measures of immediate memory.*

In general, the data supported the first hypothesis. The patients, as a group, obtained mean T scores that were significantly lower than the means of the standardization samples on five of six memory measures. The patients were also significantly more likely to obtain scores in the impaired range on these five measures. The five impaired scores were comprised of all four measures of delayed recall, as expected, plus one measure of immediate story recall. However, it is notable that this latter measure, LMI, represented the highest mean T score among the five impaired scores. On the remaining memory measure, VRI, the patients' scores were marginally lower than the normative sample.

The results indicate that persons with epilepsy who are referred for a presurgical evaluation tend to obtain below average memory test scores, and their performances tend to be more deficient on delayed recall measures than on immediate recall measures.

These findings are consistent with previous research (Breier et al., 1996; Delaney et al., 1980; Giovagnoli & Avanzini, 1996; Jones-Gotman, 1991; Loiseau et al., 1983; Randolph et al., 1994).

Hypothesis 2

> *Memory tests requiring the recollection of words or stories will be related to an underlying "verbal" memory component, and memory tests requiring the recollection of figures will be related to an underlying "visual-spatial" memory component.*

The second hypothesis was also supported. PCA revealed that the seven delayed memory measures yielded two components. As expected, the four "verbal" memory tests loaded on one factor, and the three "visual-spatial" memory tests loaded on the other factor. Therefore, two dimensions accounted for most of the variance on the seven memory tests. These dimensions appeared to reflect the verbal and the visual-spatial modalities. This result supported the validity of these tests as domain-specific measures of memory functioning. However, as is discussed below, differences other than modality of stimulus presentation might account for the two dimensions. For the purpose of the current discussion, the traditional verbal and visual-spatial terminology is retained.

By combining performances on the memory measures into two component scores, error variance was reduced and more reliable measures were produced. That is, the two components provided a more reliable method of comparing performance in the verbal and visual-spatial domains than pairs of individual memory measures. Also, the two components were more sensitive to intergroup differences than the various individual test scores. For example, the LTL and RTL groups differed significantly on the verbal memory component, whereas these two groups did not differ on any of the seven individual memory measures. Given that the goal of this study was to detect significant

correlates of memory dysfunction, the more reliable component scores served as the dependent variables in the remaining analyses.

Hypothesis 3

Duration of epilepsy, BNT score, level of depression, and level of anxiety will each account for a significant proportion of the variance in the memory component scores of the epilepsy patients.

Verbal memory component

There was little support for the third hypothesis with respect to verbal memory. The results indicated little or no linear relationship between the four predictor variables (i.e., duration, BNT score, depression, and anxiety), age, and education, and verbal memory. With regard to individual predictors, only BNT score uniquely predicted a significant, albeit small, amount of variance in verbal memory. Also, BNT score was the only variable that was significantly correlated with verbal memory component.

Naming. The relationship between BNT score and verbal memory is in agreement with previous research (Hermann et al., 1988). More specifically, persons who perform poorly on the BNT also tend to perform poorly on measures of verbal memory. This result also occurs in the normal population, and is not specific to persons with epilepsy. For example, Sewell, Downey, and Sinnett (1988) found that BNT score was significantly correlated with both verbal and visual-spatial memory in a sample of normal university students. In the current sample of presurgical epilepsy patients, both verbal memory and BNT scores appear to be generally deficient. The median scores on the BNT were below a cut-off score[23] of 51 in all patient groups except the nonsurgical group.

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[23] This cut-off score was suggested by Van Gorp, Satz, Kiersch, & Henry (1986) for well-educated 60-64-year-olds because it was 2 standard deviations below the mean of that sample. This score was also 2

Anxiety and depression. Contrary to expectation, neither depression nor anxiety predicted verbal memory performance. With regard to the effect of anxiety, Corcoran and Thompson (1993) found that anxiety was related to delayed story recall as well as other measures of memory. Differences in the characteristics of the participants and in the measures of anxiety may account for this discrepant result. For example, Corcoran and Thompson (1993) evaluated a heterogeneous sample of persons with epilepsy who were recruited via postal survey, and they used the Hospital Anxiety and Depression Scale (i.e., the anxiety scale only; HAD-A) to assess anxiety. In the present study, a selected sample of patients with poorly controlled seizures who were presenting for presurgical evaluation were evaluated, and Scale 7 of the MMPI-2 was used to assess anxiety. The HAD-A contains only 7 items related to anxiety, whereas Scale 7 of the MMPI-2 contains 48 items related to anxiety.

With regard to the effect of depression, in retrospect, the lack of a relationship between depression and the verbal memory component is not so surprising. Corcoran and Thompson (1993) found that depression was related to immediate story recall, whereas, in the present study, measures of immediate recall were not included in the calculation of the memory components. Also, there were differences in the characteristics of the participants, as noted above, and in the measures of depression. Corcoran and Thompson (1993) used the Beck Depression Inventory (BDI) to assess depression, which contains 21 items related to depression, whereas Scale 2 of the MMPI-2 was used to assess depression in the present study, which contains 57 items related to depression. In summary, based on the measures used in this study, there is no significant relationship between anxiety or depression and verbal memory performance in persons presenting at an epilepsy surgery clinic.

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standard deviations below the mean for 30-39-year-olds based on the original Goodglass & Kaplan (1983) normative data.

Duration. The failure of duration to predict verbal memory component score contradicts several previous findings (Delaney et al., 1980; Loiseau et al., 1982; Mirsky et al., 1960). However, the results of prior research in this area are mixed, and other studies did not find a significant relationship between duration and verbal memory performance (Hermann et al., 1988; Loiseau et al., 1980, 1983; Rausch et al., 1978; Scott et al., 1967). With regard to the studies that found a significant relationship, in the Mirsky et al. (1960) study, WMS MQ score was the dependent variable and it is noteworthy that this composite score did not include delayed recall trials. Loiseau et al. (1982) found that patients with longer duration demonstrated deficient verbal savings (i.e., percent retained) scores. However, they did not attempt to correlate duration and verbal memory functioning, and duration had no differential effect on raw delayed verbal recall scores. Finally, Delaney et al. (1980) found a negative correlation between duration and immediate and delayed verbal memory as well as visual-spatial memory in patients with temporal or frontal focal epilepsy. So, of the two studies in which delayed verbal memory was measured and duration was associated with at least one aspect of memory performance, only one study found a specific relationship between duration and delayed verbal memory. Therefore, closer scrutiny of previous research indicates that the evidence for a relationship between duration of epilepsy and delayed verbal memory is marginal at best. In keeping with this, there was no evidence of a relationship between duration of epilepsy and delayed verbal memory in the present study.

Age and education. It was also unexpected to find that neither age nor education were significantly related to verbal memory component. Indeed, age is such an important factor with respect to memory performance that allowances for age are routinely made when assessing memory in a clinical setting (e.g., Wechsler, 1987). This finding may be

a result of the rather restricted age range in the current sample, as the majority of patients were in the 25 to 45 years of age range.

Unilateral TL patients. Further multiple regression analyses assessed how well the four predictor variables predicted the verbal memory component scores of the patients with a unilateral TL seizure focus, after accounting for the effect of side of TL focus. These analyses indicated that none of the predictor variables, including BNT score, significantly contributed to the variance in the verbal memory component after considering the effect of side of TL focus. Thus, among persons with unilateral TL epilepsy, only the presence of a LTL focus was found to significantly predict verbal memory performance. This contradicts the findings of Hermann et al. (1992a) who found, conversely, that laterality was not a significant predictor of verbal memory performance after accounting for the effect of demographic variables and language function. These researchers also found that Visual Naming score (from the Multilingual Aphasia Examination) was significantly poorer in LTL patients when compared to RTL patients. In the present study, there was no difference between the groups on BNT score (see Table 14). Such contradictions in results are difficult to explain without further research, but they may reflect differences between the two studies with respect to the measures used to assess naming and verbal memory. The Visual Naming test contains drawings with somewhat more visual context than the BNT stimuli. It is possible that performance on the BNT is more sensitive to RTL seizure foci. In addition, Hermann et al. (1992a) utilized six indices from the California Verbal Learning Test (CVLT), whereas one verbal memory component was utilized in the present study.

Summary. The results of analyses regarding the prediction of verbal memory in persons with epilepsy indicate that (1) duration, anxiety, depression, age, and education are not associated with verbal memory, (2) among the entire epilepsy sample, poor BNT

score is the only significant unique predictor of poor verbal memory component score, (3) among persons with unilateral TL epilepsy, the presence of a LTL seizure focus is the only significant unique predictor of poor verbal memory component score, and (4) the presence of both low BNT score and poor verbal memory component score is characteristic of the entire sample and does not necessarily signify the presence of a LTL focus.

Visual-Spatial memory component

The results regarding the visual-spatial memory component, in contrast, indicated a significant linear relationship between the four predictor variables (i.e., duration, BNT score, depression, and anxiety), age, and education, and visual-spatial memory. Also, BNT score, anxiety, and age were significant unique predictors of visual-spatial memory. The relationships between depression and duration, and visual-spatial memory, appear to be mediated by, or redundant with, the relationships between BNT score, anxiety, and age, and visual-spatial memory. Given that the measures of depression and anxiety (i.e., MMPI-2 Scales 2 and 7) were highly correlated, and that 54.8% of the variance in the depression score was accounted for by the anxiety score, the most parsimonious explanation is that the measure of depression was redundant with the measure of anxiety. In addition, age accounted for 11.6% of the variance in duration, which suggested that the effect of duration was redundant with the effect of age.

Anxiety and depression. Increased level of anxiety predicted a decreased visual-spatial memory component score, whereas depression was not uniquely related to the visual-spatial memory component score. This is consistent with the findings of Corcoran and Thompson (1993) who reported that anxiety was related to design learning[24] and other measures, whereas depression was only related to immediate story recall.

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[24] They did not measure delayed visual-spatial recall.

A high score on the anxiety scale is associated with specific characteristics, including tendencies to be tense and ruminative and have difficulties concentrating, whereas these characteristics are not part of a high depression scale profile (Butcher & Williams, 1992). Increased distractibility associated with anxiety might underlie poor visual-spatial memory test performance (see Watts & Sharrock, 1985). Alternatively, a third factor related to the presence of epilepsy might underlie both increased anxiety and decreased visual-spatial memory. Finally, it is possible that poor visual-spatial memory leads to increased anxiety.

There is a general need for more research on the relationship between mood and memory test performance. In particular, it would be helpful to better understand which characteristics of mood disturbance are related to specific aspects of memory and cognitive functioning. For example, perhaps distractibility or mind-wandering is more particularly important vis-à-vis memory test performance than mood (see Watts & Sharrock, 1985).

Age and education. In agreement with normative data, age was a predictor of the visual-spatial memory component although education was not. It appears that the visual-spatial memory component is more sensitive to the effects of age than the verbal memory component. Moreover, visual-spatial memory may be more sensitive to the effects of age in the normal population (Moye, 1997). Also, age was correlated with two of the three visual-spatial memory tests, but none of the verbal memory tests (see Table 26). The results are partially consistent with those of Baxendale et al. (1998), who found that age was a significant unique predictor of delayed figure recall but not delayed story recall.

Insert Table 26 about here

Naming. Previous studies of memory performance in persons with epilepsy have not examined the relationship between BNT score and visual-spatial memory. Hence, finding that BNT performance was a significant unique predictor of visual-spatial memory in the present study was somewhat unexpected, as naming is generally considered a verbal task, and visual-spatial memory tests are designed to be non-verbal in nature. Nevertheless, there are similarities between the BNT and visual-spatial memory tests. First, the BNT and the visual-spatial memory tests both utilize visual stimuli. Second, performance on both the BNT and visual-spatial memory tests can be influenced by a variety of factors, not necessarily reflecting deficits in the domain that the test was designed to assess.

The BNT was designed to assist in the assessment of patients with aphasia (Goodglass & Kaplan, 1983). Patients with anomia obtain low scores on the BNT because of difficulty retrieving the names of the pictures. However, patients with visual-perception deficits also can obtain low scores as a result of difficulty identifying the picture. The stimuli in the BNT are not real-world photographs, but simple line drawings of objects presented without a context. Thus, for example, the drawing of a harmonica, which includes a line of small squares representing the holes through which air is blown to play the instrument, could be misperceived as a line of windows on a bus (Lezak, 1995). Also, BNT performance has been shown to be significantly related to a measure of perceptual integration (Hooper Visual Object Perception Test; Paolo, Cluff, & Ryan, 1996; Ricker & Axelrod, 1995).

Similarly, poor verbal skills can hinder performance on visual-spatial memory tests because verbalization of test stimuli can enhance performance. For example, if the first stimulus card from the WMS-R VR subtests (see Figure 3) were translated as "an X

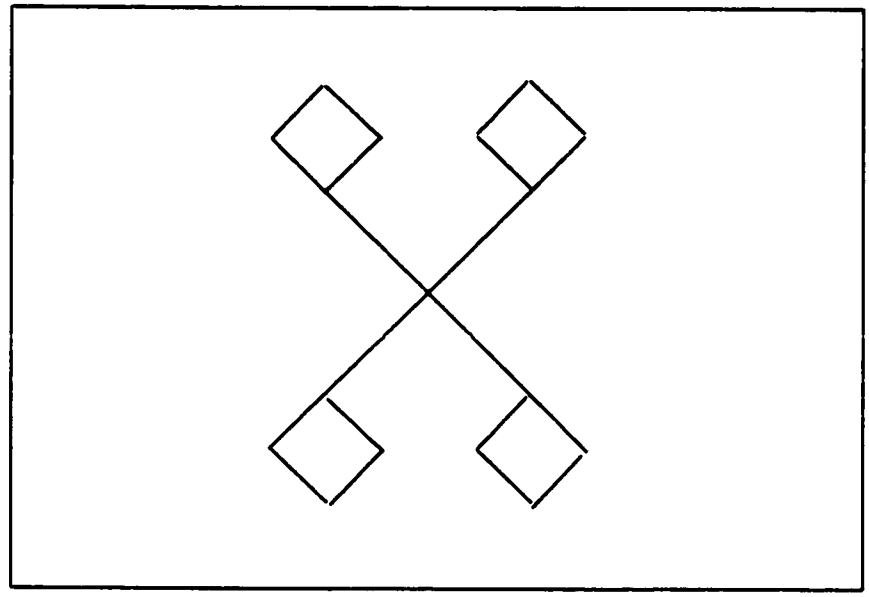

Figure 3. The first stimulus card of the WMS-R VR subtests.

with square flags at the end of each line pointing medially" one would have a good chance of reproducing it based on the verbal code alone.

There is abundant evidence in the literature to support the differential and predictive validity of the BNT, especially with respect to the presence and severity of dementia (Lezak, 1995; Spreen & Strauss, 1998). However, there is less evidence regarding the construct validity of the BNT. In one study, Sewell and colleagues (1988) evaluated how BNT was related to WMS subtests and other measures. They included the scores of a sample of normal students on the BNT, subtests of the WMS (Russell adaptation; Russell, 1975), the Information subtest of the WAIS-R, and the Quick Test of intelligence in a PCA. In their two factor solution, BNT loaded on the "verbal" component along with immediate and delayed story recall (i.e., LM), Quick Test of intelligence, and the Information subtest of the WAIS-R. The "nonverbal" component included immediate and delayed figural recall (i.e., VR), and Digit Span. These results appeared to support the distinction of the BNT as a primarily verbal test. However, it should be noted that the memory tests included by Sewell et al. (1988) in the PCA differed from those used in the present study.

To examine how well the present patient data compare with the data of normals vis-à-vis the relationship between BNT and various memory tests, a PCA that was partially analogous to the Sewell et al. (1988) analysis was conducted. The results, displayed in Table 27, are in agreement with those of Sewell et al. (1988). For the epilepsy patients in the current study, BNT loaded on the first component with the verbal memory tests, just as it did with normals.

Insert Table 27 about here

For the purpose of comparison, another PCA was conducted in which BNT was included with the seven memory measures used in the present study (see Table 28). In that analysis, BNT loaded on the visual-spatial component. Interestingly, the loadings of the LMII score were relatively ambiguous, with the higher loading on the "visual-spatial" component. Thus, BNT loaded on a visual-spatial component when it was included with the memory measures used in the present study, but loaded on a verbal component when it was included with more conventional measures of immediate and delayed recall.

Insert Table 28 about here

The choice of memory tests for the PCA appears to be a significant factor in determining the factor on which BNT loads. The most obvious difference between the PCAs in Tables 27 and 28 is that measures of immediate recall were only included in the analysis depicted in Table 27. Hence, a final PCA was conducted that included BNT, the seven memory measures chosen for this study, plus two measures of immediate recall, to examine how including measures of immediate recall might influence the result.[25] The results displayed in Table 29 show a three factor solution in which BNT loaded on a third factor with immediate and delayed story recall. The remaining "verbal" memory tests loaded on the second factor, and all "visual-spatial" memory tests loaded on the first factor. Thus, BNT score loaded with the verbal memory tests that involved retrieving information that was presented in a meaningful context. The verbal memory tests that comprised the second component involved retrieving information that was presented as unrelated words. The memory tests that loaded on the third component all involved

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[25] Two multivariate outliers were excluded from this analysis: (1) a 26-year-old female with a LTL focus, 18 years of education, and 22 years duration of epilepsy ($\chi^2 = 28.66$, $p < .001$) and (2) a 22-year-old male with RTL focus, 13 years of education, and 7 years duration of epilepsy ($\chi^2 = 30.18$, $p < .001$). The remaining assumptions of PCA were met.

retrieval of figural information. It would appear that BNT did not load on the verbal memory component of the original PCA because most of the verbal memory test scores that were included did not involve retrieval of information that was presented in a meaningful context. Furthermore, the only measure with which BNT did not significantly correlate (i.e., RAVLT-RI) loaded on the verbal memory component (see Table 30). Thus, in the original PCA, BNT shared relatively more common variance with the visual-spatial measures.

Insert Table 29 about here

Insert Table 30 about here

Duration. In the entire sample of epilepsy patients, duration was not a unique predictor of visual-spatial memory. Instead, the effect of duration appeared to be redundant with the effect of age. In contrast, within the unilateral TL subsample duration was a marginal predictor of visual-spatial memory component, whereas age was not associated with visual-spatial memory. This suggests that duration was a specific predictor of visual-spatial memory only within the unilateral TL subsample. An explanation for this pattern was not immediately obvious. However, these findings coincide with mixed results from previous studies. That is, several studies found that duration was associated with memory (Delaney et al., 1980; Loiseau et al., 1982; Mirsky et al., 1960), whereas other studies did not find a significant relationship (Hermann et al., 1988; Loiseau et al., 1980, 1983; Rausch et al., 1978; Scott et al., 1967). Moreover, Baxendale et al. (1998) found that both age and duration helped predict delayed visual-

spatial (i.e., complex figure) recall among presurgical TLE patients. There were no obvious discrepancies between the Baxendale et al. (1998) study and the present study in terms of participants, duration of epilepsy, or IQ. However, the Baxendale et al. study utilized one measure of visual-spatial recall, whereas the present study utilized a visual-spatial memory component derived from three measures. More research is required to understand the complex interaction between duration and age vis-à-vis memory functioning within specific epilepsy patient groups.

Unilateral TL patients. Further multiple regression analyses assessed how well the four predictor variables could predict the visual-spatial memory component in the unilateral TL groups, after accounting for the effect of side of TL focus. In contrast to the results for verbal memory, BNT score remained a significant predictor of visual-spatial memory, and anxiety and duration were marginally significant. Specific results regarding duration were discussed above.

Summary. The results of analyses regarding the prediction of visual-spatial memory in persons with epilepsy indicate that among the entire epilepsy sample (1) BNT score, anxiety, and age are significant unique predictors of visual-spatial memory and (2) the effects of depression and duration appear to be redundant with the effects of anxiety and age, respectively. Among the unilateral TL patients (1) side of TL focus is not related to visual-spatial memory, (2) BNT score is a significant predictor of visual-spatial memory, (3) anxiety and duration are marginal predictors of visual-spatial memory, and (4) the effect of depression appears to be redundant with the effect of anxiety. Finally, in a PCA with immediate and delayed recall measures, BNT loaded on a dimension with measures of verbal semantic retrieval. In contrast, when the inclusion of such measures was restricted, BNT loaded on a dimension with measures of visual-spatial memory. The

results with regard to hypothesis 3 may not apply to patients with very low BNT, visual-spatial memory, or Full Scale IQ scores.

Hypothesis 4

Patients with a LTL seizure focus will obtain relatively poor verbal memory component scores, whereas patients with a RTL seizure focus will obtain relatively poor visual-spatial memory component scores.

The verbal memory component scores were significantly poorer in the LTL group than the RTL group. This confirmed the first part of the fourth hypothesis and is consistent with previous findings (Breier et al., 1996; Christianson et al., 1992; Delaney et al., 1980; Giovagnoli & Avanzini, 1996; Helmstaedter et al., 1995; Hermann et al., 1987; Jones-Gotman, 1991; Làdavas et al., 1979; Masui et al., 1984; McGlone, 1994; O'Shea et al., 1996; Saykin et al., 1989; Seidenberg et al., 1993; Tröster et al., 1989, cf. Mayeux et al., 1980; Thompson & Trimble, 1996). In contrast, there were no group differences on the visual-spatial memory component score. It is notable that previous research in this area has been mixed. Most studies found that RTL focus was associated with poor visual-spatial memory (Breier et al., 1996; Delaney et al., 1980; Helmstaedter et al., 1991; Jones-Gotman, 1991; Làdavas et al., 1979), whereas some studies failed to find such a relationship (Saykin et al., 1989; Snitz et al., 1996; Thompson & Trimble, 1996).

When the data were viewed from the perspective of pattern analysis a significant interaction was found between patient group and verbal versus visual-spatial discrepancy. Patients in the LTL group were more likely to obtain higher visual-spatial component scores and patients in the RTL group were more likely to obtain higher verbal component scores. This finding fully supports the fourth hypothesis, and illustrates the importance of examining patterns among scores in neuropsychological research.

Prior studies have found that visual-spatial memory performance in RTL patients can be mediated by other factors such as gender (McGlone, 1994), or the verbal complexity of the visual stimuli (Helmstaedter et al., 1995). In the present study, gender did not interact with side of TL focus with respect to visual-spatial memory performance (ANOVA, $p > .10$). To investigate the influence of verbal complexity on visual-spatial memory performance, a more detailed examination of the present data was conducted.

The VR subtests of the WMS-R contain four items of varying complexity. The first three cards contain a single figure with a maximum score ranging from 7 to 9. The fourth card contains two figures with a maximum score of 18. If it can be presumed that it would be more difficult to verbalize the entire contents of the fourth card within 10 seconds, than to verbalize the entire contents of one of the first three cards within 10 seconds, then a person who relies upon verbalization to perform a visual-spatial memory task would have greater difficulty completely recalling the more complex card. In particular, if the RTL patients tend to verbalize figural stimuli, as has been previously suggested (Helmstaedter et al., 1995), then they would be expected to have relatively more difficulty on the fourth, more "verbally complex" card, than, say, the second, less "verbally complex" card.[26] The current data were analyzed with respect to this idea, but the results did not confirm the findings of Helmstaedter et al. (1995). Instead, the RTL and LTL groups obtained equivalent scores on the second and the fourth cards of the VRI and VRII subtests of the WMS-R (ANOVA, all $ps > .5$). It should be noted that Helmstaedter and collagues used the Benton Visual Retention Test, which may have been more sensitive to "verbal load" than the WMS-R VR subtests. In the present case, however, there is no evidence that verbal complexity interacted with side of TL focus with respect to visual-spatial memory performance.

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[26] The second card is chosen over the first card for this comparison because there is no practice trial given before the first card.

Hypothesis 5

Duration, BNT score, depression, and anxiety will each accentuate the decrement in verbal and visual-spatial memory shown by the left and right temporal lobe groups, respectively.

The fifth, and final, hypothesis was based on one previous study and represented the most exploratory hypothesis in this study. In an attempt to account for more variance in memory performance, analyses were undertaken to determine whether the four predictor variables interacted with side of TL focus vis-à-vis the memory component scores. None of these analyses were significant, and there was no evidence that any of the four predictor variables interacted with side of TL seizure focus with respect to memory performance. Thus, the finding of Làdavas et al. (1979), that longer duration was associated with a greater decrement in verbal memory for LTL patients, and a greater decrement in visual-spatial memory in RTL patients, was not replicated. However, there were a number of methodological differences between the two studies. First, in the Làdavas et al. study, patients were divided into two groups according to whether duration was greater than, or less than, one year (i.e., duration was used as a dichotomous variable). In the present study, a multiple regression method was utilized so that patients would not have to be partitioned according to duration. If artificial groups had been created according to duration, there would have been a corresponding reduction in variance accounting, power, and significance (Cohen & Cohen, 1983). Second, on average, the present sample appears to have a longer duration (mean = 19.06, SD = 11.64) than the Làdavas et al. sample (mean = 8.7 years). Third, the Làdavas et al. sample was restricted to persons with an age at onset of 10 years of age or more, whereas the present sample included persons with an age at onset ranging from infancy to 48 years

of age.[27] Fourth, Ladavas et al. compared groups on a difference score (i.e., verbal minus visual-spatial memory scores), whereas in the present study group differences were assessed on verbal and visual-spatial memory independently. In sum, the present study differs from Làdavas et al. (1979) on a number of grounds, and there is no obvious reason to suspect that the present results are erroneous. Also, there is no known report in the literature that has replicated the Làdavas et al. (1979) finding.

Conclusions related to the five hypotheses

In summary, hypotheses one, two, and four were supported, the third hypothesis was partially supported, and the fifth hypothesis was not supported. Clearly, the set of predictor variables used in this study, taken alone or in combination, failed to account for the majority of variance in memory performance of persons with epilepsy. That is, even though there were a number of statistically significant effects, factors other than side of TL focus, duration of epilepsy, BNT score, anxiety, depression, age, and/or education level accounted for a large proportion of the variance in memory performance.

A closer examination of the neurophysiological effects of seizures may increase our understanding of why persons with epilepsy consistently display poor memory performance. For example, animal studies investigating the physiological effects of recurrent focal seizures lasting several hours have found both acute and chronic sequelae. Acutely, there is a swelling of dendrites in the seizure focus and at synapses in distant pathways, as well as a dilation of axon terminals of afferent thalamic neurons projecting into the focus. Chronically, there is neuronal loss. Furthermore, generalized convulsive seizures may interrupt breathing. Cerebral oxygen requirements are increased during a seizure, making the brain, already sensitive to oxygen deficiency, particularly vulnerable

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[27] One participant had an age at onset of 60 years of age, but 99.3% of participants had an age at onset of less than or equal to 48 years of age.

(Lothman & Collins, 1990). Thus, our ability to account for memory deficits in persons with epilepsy may be enhanced by examining the extent of seizure-related neurophysiological changes in humans, as well as the effect of specific neurophysiological changes on cognitive functioning.

Sophisticated neuroimaging techniques would be necessary for investigating the effect of seizures and particular seizure foci on neurophysiology, and the effect of changes in neurophysiology on specific cognitive skills. For example, it has recently been shown that measurements of hippocampal sclerosis in persons with TL epilepsy, made using MRI technology, are related to specific aspects of memory performance (Lencz et al., 1992). In addition, measurements of rCBF in particular brain regions have been shown to be associated with particular cognitive functions (Homan et al., 1989). Future research commensurate with technical advances may better illuminate the ways in which seizures can affect specific cognitive skills.

General discussion

The results of this study showed that LTL seizure focus predicted verbal memory performance whereas side of seizure focus did not predict visual-spatial memory performance. In contrast, BNT score, anxiety, and duration of epilepsy were predictors of poor visual-spatial memory after accounting for the effect of side of TL focus, whereas none of these factors was a significant predictor of verbal memory after accounting for the effect of side of TL seizure focus. There were no published studies that examined the differential effects of these factors (i.e., anxiety, BNT score, or duration) on verbal versus visual-spatial memory in persons with epilepsy to which the present results could be compared.

The present findings may be better understood if they are placed in the context of a model of hemispheric specialization that is based on differences in neuronal

organization (Goldberg & Costa, 1981; Goldberg & Podell, 1995; Rourke, 1989). The right cerebral hemisphere consists of relatively more associative fibres in which neuronal connections tend to be more diffuse, whereas the left hemisphere contains relatively more areas with concentrations of neurons in which neuronal connections tend to be more circumscribed. These anatomical differences suggest that the neural organization of the right hemisphere is better suited to intermodal processing and the processing of novel and complex stimuli, and the left hemisphere is better suited to automatic, routinized, unimodal processing (e.g., such as language; see Goldberg & Costa, 1981 for evidence supporting this model).

Verbal and visual-spatial memory tests can be viewed from a *"novelty-routinization"* perspective (Goldberg & Podell, 1995, p. 85). Most individuals will have had vastly more experience processing information in the verbal domain than in the visual-spatial domain. Indeed, language is the mode of most daily interactions, whereas persons rarely communicate solely through the use of figures and drawings. Thus, the assessment of memory using verbal or language-based material utilizes a well-practiced and routinized system of cognitive processing using stored codes (i.e., words).[28] According to the above model of hemispheric specialization, areas in the left hemisphere are particularly suited to this type of unimodal processing. In contrast, memory testing using figural material presents a relatively novel situation for which there are rarely stored, routinized codes readily available. Therefore a new "descriptive system" must be developed and used to process and remember the figures (Goldberg & Costa, 1981, p.

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[28] The automaticity of verbal processing is illustrated by the Stroop effect. When persons are presented with a series of colour labels printed in black ink (e.g., RED, BLUE, GREEN) the colour labels can be read aloud without difficulty. However, if the labels are printed in contrasting colours of ink it is relatively difficult to name the colour of the ink and ignore the printed labels. The tendency to automatically read the label has to be inhibited in order to focus on the ink colour (Dodrill, 1978; Stroop, 1935).

151). According to the model under consideration, the right cerebral hemisphere appears to be particularly suited for this type of processing.[29]

A right hemisphere disturbance would be expected to interfere with the integrative, intermodal processing of novel information that is associated with that cerebral hemisphere. In addition, a disturbance affecting general cognitive efficiency would be expected to disrupt the integrative, intermodal processing of novel information associated with the right hemisphere to a greater degree than the automatic, routinized processes associated with the specialized areas of the left hemisphere. Therefore, if a RTL seizure focus had an effect on memory functioning, it would be expected to affect performance in the novel (i.e., visual-spatial) domain to a greater degree than performance in the routinized (i.e., verbal) domain. Similarly, factors such as anxiety, age, and duration, would seem more likely to be related to general cognitive efficiency than a specific routinized cognitive function. If this were the case, such factors would also be expected to affect memory performance in the novel (i.e., visual-spatial) domain to a greater degree than memory performance in the routinized (i.e., verbal) domain.

Dysfunction in a specific area of the left hemisphere associated with routinized, unimodal, processing (e.g., language) would be expected to disrupt the specific cognitive processing associated with that area to a greater degree than any other cognitive function. Therefore, if a seizure focus in the LTL had an effect on memory functioning, it would be expected to affect performance in the routinized (i.e., verbal) domain to a greater degree than performance in the novel (i.e., visual-spatial) domain.

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[29] Differences in the novelty of material may account for the relative ease at which verbal material is reproduced. For example, Masui et al. (1984) attempted to assess verbal and visual-spatial recognition memory in persons with TL epilepsy using tachistoscopic presentation of words and figures, but found that performance was so poor in the visual-spatial modality that it could not be tested reliably. Testing in the verbal modality is likely easier because verbal processing is a well-rehearsed and automatic function.

The results of the present study fit the expectations of the novelty-routinization perspective. Memory performance in the verbal/routinized domain was associated with a seizure focus in the area that appears to be involved in routinized, unimodal processing – the LTL. Memory performance in the visual-spatial/novel domain was not significantly associated with side of seizure focus, although the trends illustrated in Figure 2 indicate that persons with either a focus in the RTL or an undetermined focus – i.e., outside the specialized areas of the left hemisphere or at least not detected in that area – obtained relatively poorer visual-spatial memory component scores. Furthermore, anxiety, and age or duration of epilepsy were significantly related to memory performance in the visual-spatial/novel domain, whereas, after accounting for the effect of LTL focus, none of these factors influenced memory performance in the verbal/routinized domain.

The results regarding BNT score require further elaboration. BNT score appears to be related to the relatively routinized task of word retrieval (Goodglass & Kaplan, 1983) as well as the relatively novel task of perceptual integration (Paolo et al., 1996; Ricker & Axelrod, 1995), and it is sensitive to overall cognitive decline (Spreen & Strauss, 1991). Accordingly, when the entire epilepsy sample was included, BNT score was a significant predictor of both the verbal/routinized and the visual-spatial/novel memory component scores. However, within the unilateral TL subsample, after accounting for side of TL focus, BNT score was not significantly correlated with verbal/routinized memory component score, whereas BNT score was a significant predictor of the visual-spatial/novel memory component score. Also, given the results of the PCA presented in Table 28, BNT score appears to share more common variance with the visual-spatial/novel memory component score than the verbal/routinized memory component score. Taken together, these results suggest that the BNT is not simply a measure of routinized word retrieval. The simple line drawings used as stimuli in the

BNT may represent novel material requiring integrative multimodal processing. More research is needed to determine how performance on the BNT is related to verbal skills versus general cognitive efficiency in normals and in particular patient groups.

Limitations of this study

The present patient sample was not representative of the population of persons with epilepsy. It was a highly selected sample of persons with poorly controlled seizures who presented as potential candidates for neurosurgery. As such, the results regarding the predictors of memory component scores (see hypothesis 3) do not necessarily generalize to all persons with epilepsy. On the other hand, a number of significant results were obtained by comparing the LTL and RTL patient groups within this selected group of persons with epilepsy.

There were a number of methodological limitations due to the retrospective nature of this study. First, there was no opportunity to measure or control serum anticonvulsant levels. However, as discussed in the literature review, there is little empirical evidence to suggest that anticonvulsants within therapeutic levels have a significant effect on memory performance. Second, measurements of duration of epilepsy, age at onset, seizure frequency, and etiology were gleaned from medical records and the reliability of these measures could not be checked. Third, there was no opportunity to examine the relationship between specific neuropathology and memory functioning. It has already been suggested that future research should provide a closer examination of the neuropathological effects of seizures and how they may effect memory functioning. Fourth, MMPI-2 scores were used to measure levels of depression and anxiety because they were available. Measures of depression and anxiety that were more specifically tailored to the needs of present study would have been desirable. Finally, a sizable minority of patients were tested as inpatients while they were undergoing 24 video EEG,

often with reduced AED levels. An ANOVA ruled out an interaction between testing location and side of TL seizure focus on memory component scores. Nevertheless, there were no data available regarding patient AED levels as inpatients or as outpatients.

The aim of the present study was to determine significant correlates of poor memory in persons with epilepsy and the largest possible number of participants was desired. Hence, few restrictions were placed on patient selection. That is, there were no restrictions regarding handedness, speech dominance, or presence of structural brain lesions. Many previous studies restricted patient selection to right-handed persons, persons with left hemisphere speech dominance, persons with no evidence of structural brain lesion, and/or persons who later had neurosurgery in order to keep the patient sample as homogeneous as possible. Notably, in the present sample, there were no significant relationships between handedness, speech dominance, presence/absence of brain lesion, or presence/absence of later neurosurgery and the memory component scores (all ps > .10).

Conclusion and future direction

The present study was undertaken to examine the relationship between several factors and memory functioning in the verbal/routinized and visual-spatial/novel domains in persons with epilepsy. Sensitive indices of memory functioning in each domain were computed to improve detection of significant effects. It was hoped that the results of the present study would lay the groundwork for future studies in which the goal is a more detailed analysis of various facets of memory functioning in persons with epilepsy.

The results clearly showed that poor verbal memory functioning is related to a LTL seizure focus. Poor visual-spatial memory functioning could be related to many factors, but likely not LTL seizure focus. Psychosocial factors may be related to memory

functioning in persons with epilepsy, but only with respect to memory of visual-spatial or novel information.

None of the five independent measures, alone or in combination, accounted for a majority of the variance in memory functioning in these patients. Nevertheless, the findings illustrated in Figure 1 indicate that, indeed, memory is deficient among these patients. Thus, factors other than those measured in this study also appear to be important vis-à-vis memory functioning in persons with epilepsy. For example, the mere presence of seizures may have a significant effect on memory functioning.

The results illustrated how the experiences of persons with epilepsy can contribute to improving our understanding of brain–behaviour relationships. In order to take advantage of the information that can be provided by these patients, a more comprehensive, prospective approach to research in this area is advocated. Suggestions made in the discussion regarding topics for future studies are summarized in Table 31.

Insert Table 31 about here

It would seem that the neurobiological, cognitive, and psychosocial factors examined in this study are not the key causes of the memory problems experienced by persons with epilepsy. However, such factors have been the subject of study because they are tangible variables that can be measured. It seems necessary to consider that further research of this type would be redundant unless new ways of measuring other factors are developed.

In order to make significant progress in this area, it would seem important to shift emphasis to factors such as the neurochemical and electrical changes in the brain that are associated with seizure activity. However, at this point technology has not advanced to a

state that will allow sensitive measurement of such changes. Also, our knowledge of the neurochemical and electrical underpinnings of normal memory functioning and, indeed, consciousness is inadequate. It seems that progress in this two areas would be necessary before any breakthrough in our understanding of how persons who suffer from seizures come to experience memory problems can be made.

References

Adams, K. M., Brown, G. G., & Grant, I. (1985). Analysis of covariance as a remedy for demographic mismatch of research subject groups: Some sobering simulations. Journal of Clinical and Experimental Neuropsychology, 7(4), 445-462.

Adams, R. D., & Victor, M. (1993). Principles of neurology (5th ed.). New York: McGraw Hill.

Andrewes, D. G., Bullen, J. G., Tomlinson, L., Elwes, R. D. C., & Reynolds, E. H. (1986). A comparative study of the cognitive effects of phenytoin and carbamazepine in new referrals with epilepsy. Epilepsia, 27, 128-134.

Andrewes, D. G., Puce, A., & Bladin, P. F. (1990). Post-ictal recognition memory predicts laterality of temporal lobe seizure focus: Comparison with post-operative data. Neuropsychologia, 28(9), 957-967.

Andrewes, D. G., Tomlinson, L., Elwes, R. D. C., & Reynolds, E. H. (1984). The influence of carbamazepine and phenytoin on memory and other aspects of cognitive function in new referrals with epilepsy. Acta Neurologica Scandinavica, 69(Suppl 99), 23-30.

Ayd, F. J. (1995). Lexicon of psychiatry, neurology, and the neurosciences. Baltimore, Maryland: Williams & Wilkins.

Baxendale, S. A. (1995). The hippocampus: Functional and structural correlations. Seizure, 4, 105-117.

Baxendale, S. A., Cook, M., Shorvon, S., Thompson, P. J., & Warrington, E. K. (1994). Relationship between the extent and morphology of hippocampal sclerosis and neuropsychological function. Epilepsia, 35(Suppl. 7), 28.

Baxendale, S. A., van Paesschen, W., Thompson, P. J., Connelly, A., Duncan, J. S., Harkness, W. F., & Shorvon, S. D. (1998). The relationship between quantitative MRI and neuropsychological functioning in temporal lobe epilepsy. Epilepsia, 39(2), 158-166.

Bennett, T. L. (1992). Cognitive effects of epilepsy and anticonvulsant medications. In T. L. Bennett (Eds.), The neuropsychology of epilepsy (pp. 73-95). New York: Plenum Press.

Bornstein, R. A., Pakalnis, A., Drake, M. E., & Suga, L. J. (1988). Effects of seizure type and waveform abnormality on memory and attention. Archives of Neurology, 45, 884-887.

Breier, J. I., Plenger, P. M., Wheless, J. W., Thomas, A. B., Brookshire, B. L., Curtis, V. L., Papanicolaou, A., Willmore, L. J., & Clifton, G. L. (1996). Memory tests distinguish between patients with focal temporal and extratemporal lobe epilepsy. Epilepsia, 37(2), 165-170.

Brittain, H. (1980). Epilepsy and intellectual functions. In B. M. Kulig, H. Meinardi, & G. Stores (Eds.), Epilepsy and behaviour (pp. 2-13). Lisse: Swets Zeitlinger.

Buchwald, J., & Devinsky, O. (1988). J. Russell Reynolds and the study of interictal symptoms in epilepsy. Archives of Neurology, 45, 802-803.

Butcher, J.N., & Williams, C.L. (1992). Essentials of MMPI-2 and MMPI-A interpretation. Minneapolis: University of Minnesota Press.

Calev, A., Korin, Y., Shapira, B., Kugelmass, S., & Lerer, B. (1986). Verbal and non-verbal recall by depressed and euthymic affective patients. Psychological Medicine, 16, 789-794.

Christianson, S. (1994). Comments on neuropsychological evaluation of epilepsy surgery: Are the tests sensitive enough? Acta Neurologica Scandinavica, 89(Suppl 152), 204-209.

Christianson, S.-Å., Nilsson, L.-G., Säisä, J., & Silfvenius, H. (1992). Visual half-field testing of memory functions in patients considered for surgical treatment of intractable complex partial epilepsy. Acta Neurologica Scandinavica, 86, 545-554.

Cohen, J., & Cohen, P. (1983). Applied multiple regression / correlation analysis for the behavioral sciences. 2nd edition. New York: Erlbaum.

Commission on Classification and Terminology of the International League Against Epilepsy (1981). Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia, 22, 489-501.

Commission on Classification and Terminology of the International League Against Epilepsy (1989). Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia, 30(4), 389-399.

Corcoran, R., & Thompson, P. (1992). Memory failure in epilepsy: Retrospective reports and prospective recordings. Seizure, 1, 37-42.

Corcoran, R., & Thompson, P. (1993). Epilepsy and poor memory: Who complains and what do they mean? British Journal of Clinical Psychology, 32, 199-208.

Coughlan, A. K., & Hollows, S. E. (1985). Adult Memory and Information Processing Battery (AMIPB) Test Manual. Leeds: Coughlan.

Delaney, R. C., Prevey, M. L., & Mattson, R. H. (1982). Short term retention with lateralized temporal lobe epilepsy. Cortex, 22, 591-600.

Delaney, R. C., Rosen, A. J., Mattson, R. H., & Novelly, R. A. (1980). Memory function in focal epilepsy: A comparison of non-surgical unilateral temporal lobe and frontal lobe samples. Cortex, 16, 103-117.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). California Verbal Learning Test: Adult version. San Antonio, TX: The Psychological Corporation.

DeLorenzo, R. J., & Towne, A. R. (1989). Epilepsy. In S. H. Appel (Eds.), Current neurology (pp. 27-76). Chicago: Year Book.

Dodrill, C. B. (1978). A neuropsychological battery for epilepsy. Epilepsia, 19, 611-623.

Dodrill, C. B. (1983). Psychosocial characteristics of epileptic patients. In A. A. Ward, J. K. Penry, & D. Purpura (Eds.), Epilepsy (pp. 341-353). New York: Raven Press.

Dodrill, C. B. (1986). Correlates of generalized tonic-clonic seizures with intellectual, neuropsychological, emotional, and social function in patients with epilepsy. Epilepsia, 27(4), 399-411.

Dodrill, C. B. (1988). Neuropsychology. In Laidlaw, Richens, & Chadwick (Eds.), A textbook of epilepsy (pp. 459-475).

Dodrill, C. B., & Batzel, L. W. (1986). Interictal behavioral features of patients with epilepsy. Epilepsia, 27 (Suppl. 2), S64-S76.

Dodrill, C. B., & Temkin, N. R. (1989). Motor speed is a contaminating factor in evaluating the "cognitive" effects of phenytoin. Epilepsia, 30(4), 453-457.

Dodrill, C. B., & Troupin, A. S. (1977). Psychotropic effects of carbamazepine in epilepsy: A double-blind comparison with phenytoin. Neurology, 27, 1023-1028.

Dreifuss, F. E. (1992). Cognitive function - Victim of disease or hostage to treatment? Epilepsia, 33(Suppl 1), S7-S12.

Duncan, J. S., Shorvon, S. D., & Trimble, M. R. (1990). Effects of removal of phenytoin, carbamazepine, and valproate on cognitive function. Epilepsia, 31(5), 584-591.

Durwen, H. F., & Elger, C. E. (1993). Verbal learning differences in epileptic patients with left and right temporal lobe foci - a pharmacologically induced phenomenon? Acta Neurologica Scandinavica, 87, 1-8.

Durwen, H. F., Hufnagel, A., & Elger, C. E. (1992). Anticonvulsant drugs affect particular steps of verbal memory processing - An evaluation of 13 patients with intractable complex partial seizures of left temporal lobe origin. Neuropsychologia, 30(7), 623-631.

Ercoli, L. M., Heaton, R. K., Peterkin, J. J., & Zisook, S. (1993). Minimal neuropsychological impairment associated with major depressive disorder. Convention of the American Psychological Association.

Falconer, M. A. (1971). Genetic and related aetiological factors in temporal lobe epilepsy: A review. Epilepsia, 12, 12-31.

Frisk, V., & Milner, B. (1990). The relationship of working memory to the immediate recall of stories following unilateral temporal or frontal lobectomy. Neuropsychologia, 28(2), 121-135.

Gallassi, R., Lorusso, S., Stracciari, A., Morreale, A., Procaccianti, G., & Baruzzi, A. (1986). Withdrawal of phenobarbital and carbamazepine in epileptic patients: a preliminary neuropsychological report. Acta Neurologica Scandinavica, 74, 59-62.

Gallassi, R., Morreale, A., Di Sarro, R., Marra, M., Lugaresi, E., & Baruzzi, A. (1992). Cognitive effects of antiepileptic drug discontinuation. Epilepsia, 33(Suppl 6), S41-S44.

Gallassi, R., Morreale, A., Lorusso, S., Ferrari, M., Procaccianti, G., Lugaresi, E., & Baruzzi, A. (1987). Cognitive effects of phenytoin during monotherapy and after withdrawal. Acta Neurologica Scandinavica, 75, 258-261.

Gallassi, R., Morreale, A., Lorusso, S., Procaccianti, G., Lugaresi, E., & Baruzzi, A. (1988). Carbamazepine and phenytoin: Comparison of cognitive effects in epileptic patients during monotherapy and withdrawal. Archives of Neurology, 45, 892-894.

Giovagnoli, A. R., & Avanzini, G. (1996). Forgetting rate and interference effects on a verbal memory distractor task in patients with temporal lobe epilepsy. Journal of Clinical and Experimental Neuropsychology, 18(2), 259-264.

Glowinski, H. (1973). Cognitive deficits in temporal lobe epilepsy. The Journal of Nervous and Mental Disease, 157(2), 129-137.

Goldberg, E., & Costa, L. D. (1981). Hemisphere differences in the acquisition and use of descriptive systems. Brain and Language, 14, 144-173.

Goldberg, E., & Podell, K. (1995). Lateralization in the frontal lobes. Advances in Neurology, 66, 85-96.

Goodglass, H. & Kaplan, E. (1983). The assessment of aphasia and related disorders (2nd ed.). Philadelphia: Lea & Febiger.

Grady, D. A., & Seebauer, E. (1993). Attention and memory in adult unipolar, non-psychotic depressed inpatients. Convention of the American Psychological Association.

Halgren, E., Stapleton, J., Domalski, P., Swartz, B. E., Delgado-Escueta, A. V., Walsh, G. O., Mandelkern, M., Blahd, W., & Ropchan, J. (1991). Memory dysfunction in epilepsy patients as a derangement of normal physiology. Advances in Neurology, 55, 385-410.

Hathaway, S. R., & McKinley, J. C. (1989). Minnesota Multiphasic Personality Inventory - 2 Manual. University of Minnesota Press.

Hauser, W. A., Annegers, J. F., & Anderson, V. E. (1983). Epidemiology and the genetics of epilepsy. In A. A. Ward, J. K. Penry, & D. Purpura (Eds.), Epilepsy (pp. 267-277). New York: Raven Press.

Haynes, S. D., & Bennett, T. L. (1992). Historical perspective and overview. In T. L. Bennett (Eds.), The neuropsychology of epilepsy (pp. 3-15). New York: Plenum Press.

Helmstaedter, C., Pohl, C., & Elger, C. E. (1995). Relations between verbal and nonverbal memory performance: Evidence of confounding effects particularly in patients with right temporal lobe epilepsy. Cortex, 31, 345-355.

Helmstaedter, C., Pohl, C., Hufnagel, A., & Elger, C. E. (1991). Visual learning deficits in nonresected patients with right temporal lobe epilepsy. Cortex, 27, 547-555.

Hermann, B. P., Connell, B., Barr, W. B., & Wyler, A. R. (1995). The utility of the Warring Recognition Memory Test for temporal lobe epilepsy: Pre- and postoperative results. Journal of Epilepsy, 8, 139-145.

Hermann, B. P., Seidenberg, M., Haltiner, A., & Wyler, A. R. (1992a). Adequacy of language function and verbal memory performance in unilateral temporal lobe epilepsy. Cortex, 28, 423-433.

Hermann, B. P., & Whitman, S. (1984). Behavioral and personality correlates of epilepsy: A review, methodological critique, and conceptual model. Psychological Bulletin, 95(3), 451-497.

Hermann, B. P., & Whitman, S. (1991). Neurobiological, psychosocial, and pharmacological factors underlying interictal psychopathology in epilepsy. Advances in Neurology, 55, 439-452.

Hermann, B. P., Whitman, S., & Anton, M. (1992b). A multietiological model of psychological and social dysfunction in epilepsy. In T. L. Bennett (Eds.), The neuropsychology of epilepsy (pp. 39-57). New York: Plenum Press.

Hermann, B., Wyler, A., Richey, E., & Rea, J. (1987). Memory function and verbal learning ability in patients with complex partial seizures of temporal lobe origin. Epilepsia, 28, 547-554.

Hermann, B. P., Wyler, A. R., Steenman, H., & Richey, E. T. (1988). The interrelationship between language function and verbal learning/memory performance in patients with complex partial seizures. Cortex, 24, 245-253.

Hertel, P. T., & Rude, S. S. (1991). Recalling in a state of natural or experimental depression. Cognitive Therapy and Research, 15(2), 103-127.

Hill, R. D., & Vandervoort, D. (1992). The effects of state anxiety on recall performance in older learners. Educational Gerontology, 18(6), 597-605.

Homan, R. W., Paulman, R. G., Devous, M. D., Walker, P., Jennings, L. W., & Bonte, F. J. (1989). Cognitive function and regional cerebral blood flow in partial seizures. Archives of Neurology, 46, 964-970.

Incisa Della Rocchetta, A., & Milner, B. (1993). Strategic search and retrieval inhibition -- the role of the frontal lobes. Neuropsychologia, 31(6), 503-524.

Incisa della Rocchetta, A., Gadian, D. G., Connelly, A., Polkey, C. E., Jackson, G. D., Watkins, K. E., Johnson, C. L., Mishkin, M., & Vargha-Khadem, F. (1995). Verbal memory impairment after right temporal lobe surgery: Role of contralateral damage as revealed by ^{1}H magnetic resonance spectroscopy and T_2 relaxometry. Neurology, 45, 797-802.

Jones-Gotman, M. (1991). Localization of lesions by neuropsychological testing. Epilepsia, 32(Suppl. 5), S41-S52.

Kälviäinen, R., Partanen, K., Äikiä, M., Mervaala, E., Vainio, P., Riekkinen, S., P.J., & Pitkänen, A. (1997). MRI-based hippocampal volumetry and T_2 relaxometry: Correlation to verbal memory performance in newly diagnosed epilepsy patients with left-sided temporal lobe focus. Neurology, 48, 286-287.

Kandel, E. R. (1991). Brain and behavior. In E. R. Kandell, J. H. Schwartz, & T. M. Jessell (Eds.), Principles of neural science (pp. 5-16). New York: Elsevier.

Kaplan, E. F., Goodglass, H., & Weintraub, S. (1983). The Boston Naming Test. Boston: Kaplan & Goodglass.

Kapur, N. (1994). Memory disorders in clinical practice. Hove, UK: Lawrence Erlbaum.

Kimura, D. (1963). Right temporal lobe damage. Archives of Neurology, 8, 264-271.

Làdavas, E., Umiltà, C., & Provinciali, L. (1979). Hemisphere-dependent cognitive performances in epileptic patients. Epilepsia, 20, 493-502.

Larrabee, G. J. (1987). Further cautions in interpretation of comparisons between the WAIS-R and the Wechsler Memory Scale. Journal of Clinical and Experimental Neuropsychology, 9(4), 456-460.

Lencz, T., McCarthy, G., Bronen, R. A., Scott, T. M., Inserni, J. A., Sass, K. J., Novelly, R.A., Kim, J. H., & Spencer, D. D. (1992). Quantitative magnetic resonance imaging in temporal lobe epilepsy: Relationship to neuropathology and neuropsychological function. Annals of Neurology, 31, 629-637.

Lennox, W. G., & Lennox, M. A. (1960). Epilepsy and related disorders. Boston: Little, Brown and Co.

Levin, R., Banks, S., & Berg, B. (1988). Psychosocial dimension of epilepsy: a review of the literature. Epilepsia, 29, 805-816.

Lezak, M. D. (1995). Neuropsychological assessment (3rd ed.). New York: Oxford University Press.

Loiseau, P., Signoret, J. L., & Strube, E. (1984). Attention problems in adult epileptic patients. Acta Neurologica Scandinavica, 69(Suppl 99), 31-34.

Loiseau, P., Signoret, J. L., Strube, E., Broustet, D., & Dartigues, J. F. (1982). Nouveaux procédés d'appréciation des troubles de la mémoire chez les épileptiques. Revue Neurologique, 138(5), 387-400.

Loiseau, P., Strube, E., & Signoret, J.-L. (1988). Memory and epilepsy. In M. R. Trimble & Reynolds (Eds.), Epilepsy, Behaviour, and Cognitive Function (pp. 165-176).

Loiseau, P., Strube, E., Broustet, D., Battellochi, S., Gomeni, C., & Morselli, P. L. (1980). Evaluation of memory function in a population of epileptic patients and matched controls. Acta Neurologica Scandinavica, 62(Suppl. 80), 58-61.

Loiseau, P., Strube, E., Broustet, D., Battellochi, S., Gomeni, C., & Morselli, P. L. (1983). Learning impairment in epileptic patients. Epilepsia, 24, 183-192.

Lothman, E. W., & Collins, R. C. (1990). Seizures and epilepsy. In A. L. Pearlman & R. C. Collins (Eds.), Neurobiology of disease (pp. 276-298). New York: Oxford University Press.

Ludgate, J., Keating, J., O'Dwyer, R., & Callaghan, N. (1985). An improvement in cognitive function following polypharmacy reduction in a group of epileptic patients. Acta Neurological Scandinavica, 71, 448-452.

Massman, P. J., Delis, D. C., Butters, N., Dupont, & Gillin (1992). The subcortical dysfunction model of memory deficits in depression: Neuropsychological validation in a subgroup of patients. Journal of Clinical and Experimental Neuropsychology, 14, 687-706.

Masui, K., Niwa, S.-I., Anzai, N., Kameyama, T., Saitoh, O., & Rymar, K. (1984). Verbal memory disturbances in left temporal lobe epileptics. Cortex, 20, 361-368.

Mayeux, R., Brandt, J., Rosen, J., & Benson, D. F. (1980). Interictal memory and language impairment in temporal lobe epilepsy. Neurology, 30, 120-125.

McGlone, J. (1994). Memory complaints before and after temporal lobectomy: Do they predict memory performance or lesion laterality? Epilepsia, 35((3)), 529-539.

McIntosh, G. C. (1992a). Medical treatment of epilepsy. In T. L. Bennett (Eds.), The neuropsychology of epilepsy (pp. 201-212). New York: Plenum Press.

McIntosh, G. C. (1992b). Neurological conceptualizations of epilepsy. In T. L. Bennett (Eds.), The neuropsychology of epilepsy (pp. 17-37). New York: Plenum Press.

McMillan, T. M., Powell, G. E., Janota, I., & Polkey, C. E. (1987). Relationships between neuropathology and cognitive functioning in temporal lobectomy patients. Journal of Neurology, Neurosurgery, and Psychiatry, 50, 167-176.

Meador, K. J., Loring, D. W., Huh, K., Gallagher, B. B., & King, D. W. (1990). Comparative cognitive effects of anticonvulsants. Neurology, 40, 391-394.

Mendez, M. F., Cummings, J. L., & Benson, D. F. (1986). Depression in epilepsy: Significance and phenomenology. Archives of Neurology, 43, 766-770.

Miller, L. A., Muñoz, D. G., & Finmore, M. (1993). Hippocampal sclerosis and human memory. Archives of Neurology, 50, 391-394.

Milner, B. (1971). Interhemispheric differences in the localization of psychological processes in man. British Medical Bulletin, 27(3), 272-277.

Mirsky, A. F., Primac, D. W., Marsan, C. A., Rosvold, H. E., & Stevens, J. R. (1960). A comparison of the psychological test performance of patients with focal and nonfocal epilepsy. Experimental Neurology, 2, 75-79.

Moscovitch, M. (1992). A neuropsychological model of memory and consciousness. In L. R. Squire & N. Butters (Eds.), Neuropsychology of memory (pp. 5-22). New York: Guilford Press.

Moye, J. (1997). Nonverbal memory assessment with designs: Construct validity and clinical utility. Neuropsychology Review, 7, 157-170.

Mungas, D., Ehlers, C., Walton, N., & McCutchen, C. B. (1985). Verbal learning differences in epileptic patients with left and right temporal lobe foci. Epilepsia, 26(4), 340-345.

Nilsson, L., Christianson, S., Silfvenius, H., & Blom, S. (1984). Preoperative and postoperative memory testing of epileptic patients. Acta Neurologica Scandinavica, 69(Suppl 99), 43-56.

Norman, R. M., Sandry, S., & Corsellis, J. A. N. (1974). The nature and origin of pathoanatomical change in the epileptic brain. In Virkin & Bruyn (Eds.), Handbook of Clinical Neurology (pp. 611-620).

O'Shea, M. F., Saling, M. M., Bladin, P. F., & Berkovic, S. F. (1996). Does naming contribute to memory self-report in temporal lobe epilepsy? Journal of Clinical and Experimental Neuropsychology, 18(1), 98-109.

Pedhazur, E. (1982). Multiple Regression in Behavioral Research (2nd ed.) New York: Holt Rinehart Winston.

Perrine, K., Hermann, B. P., Meador, K. J., Vickrey, B. G., Cramer, J. A., Hays, R. D., & Devinsky, O. (1995). The relationship of neuropsychological functioning to quality of life in epilepsy. Archives of Neurology, 52, 997-1003.

Posner, M. I., & Boies, S. J. (1971). Components of attention. Psychological Review, 78(5), 391-408.

Powell, G. E., Sutherland, G., & Agu, G. A. (1984). Serial position, rehearsal and recall in temporal lobe epilepsy. British Journal of Clinical Psychology, 23, 153-154.

Prevey, M. L., Delaney, R. C., & Mattson, R. H. (1988). Metamemory in temporal lobe epilepsy: Self-monitoring of memory functions. Brain and Cognition, 7, 298-311.

Prevey, M. L., Delaney, R. C., Mattson, R. H., & Tice, D. M. (1991). Feeling-of-knowing in temporal lobe epilepsy: Monitoring knowledge inaccessible to conscious recall. Cortex, 27, 81-92.

Prevey, M. L., Mattson, R. H., & Cramer, J. A. (1989). Improvement in cognitive functioning and mood state after conversion to valproate monotherapy. Neurology, 39, 1640-1641.

Prigatano, G. P. (1978). Wechsler Memory Scale: A selective review of the literature. Journal of Clinical Psychology, 34, 816-832.

Pulliainen, V., & Jokelainen, M. (1994). Effects of phenytoin and carbamazepine on cognitive functions in newly diagnosed epileptic patients. Acta Neurologica Scandinavica, 89, 81-86.

Randolph, C., Gold, J. M., Kozora, E., Cullum, C. M., Hermann, B. P., & Wyler, A. R. (1994). Estimating Memory Function: Disparity of Wechsler Memory Scale - Revised and California Verbal Learning Test indices in clinical and normal samples. The Clinical Neuropsychologist, 8(1), 99-108.

Rausch, R., & Babb, T. L. (1993). Hippocampal neuron loss and memory scores before and after temporal lobe surgery for epilepsy. Archives of Neurology, 50, 812-817.

Rausch, R., Lieb, J. P., & Crandall, P. H. (1978). Neuropsychologic correlates of depth spike activity in epileptic patients. Archives of Neurology, 35, 699-776.

Reitan, R. M., & Wolfson, D. (1993). The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation. South Tucson, Arizona: Neuropsychology Press.

Ricker, J.H. & Axelrod, B.N. (1995). Hooper Visual Organization Test: Effects of object naming ability. The Clinical Neuropsychologist, 9, 57-62.

Robertson, M. M. (1991). Depression in epilepsy. In M. R. Trimble (Eds.), Women and epilepsy (pp. 223-242). Wiley.

Robertson, M. M., Trimble, M. R., & Townsend, H. R. A. (1987). Phenomenology of depression in epilepsy. Epilepsia, 28(4), 364-372.

Rourke, B. P. (1989). Nonverbal learning disabilities: The syndrome and the model. New York: Guilford Press.

Russell, E. W. (1975). A multiple scoring method for the assessment of complex memory functions. Journal of Consulting and Clinical Psychology, 43(6), 800-809.

Saling, M. M., Berkovic, S. F., O'Shea, M. F., Kalnins, R. M., Darby, D. G., & Bladin, P. F. (1993). Lateralization of verbal memory and unilateral hippocampal sclerosis: Evidence of task-specific effects. Journal of Clinical and Experimental Neuropsychology, 15(4), 608-618.

Sass, K. J., Buchanan, C. P., Kraemer, S., Westerveld, M., Kim, J. H., & Spencer, D. D. (1995). Verbal memory impairment resulting from hippocampal neuron loss among epileptic patients with structural lesions. Neurology, 45, 2154-2158.

Sass, K. J., Sass, A., Westerveld, M., Lencz, T., Novelly, R. A., Kim, J. H., & Spencer, D. D. (1992). Specificity in the correlation of verbal memory and hippocampal neuron loss: Dissociation of memory, language, and verbal intellectual ability. Journal of Clinical and Experimental Neuropsychology, 14(5), 662-672.

Sass, K. J., Spencer, D. D., Kim, J. H., Westerveld, M., Novelly, R. A., & Lencz, T. (1990). Verbal memory impairment correlates with hippocampal pyramidal cell density. Neurology, 40, 1694-1697.

Saykin, A. J., Gur, R. C., Sussman, N. M., O'Connor, M. J., & Gur, R. E. (1989). Memory deficits before and after temporal lobectomy: Effect of laterality and age of onset. Brain and Cognition, 9, 191-200.

Schwartz, M. L., & Dennerll, R. D. (1969). Immediate visual memory as a function of epileptic seizure type. Cortex, 5, 69-74.

Scott, D. F., Moffett, A., Mathews, A., & Ettlinger, G. (1967). The effect of epileptic discharges on learning and memory in patients. Epilepsia, 8, 188-194.

Seidenberg, M., Hermann, B., Haltiner, A., & Wyler, A. (1993). Verbal recognition memory performance in unilateral temporal lobe epilepsy. Brain and Language, 44, 191-200.

Sewell, K. W., Downey, R. G., & Sinnett, E. R. (1988). Convergence and divergence of clinical memory tests. Psychological Reports, 62, 291-197.

Smith, D. B. (1991). Cognitive effects of antiepileptic drugs. Advances in Neurology, 55, 197-212.

Snitz, B. E., Roman, D. D., & Beniak, T. E. (1996). Efficacy of the Continuous Visual Memory Test in Lateralizing Temporal Lobe Dysfunction in Chronic Complex-Partial Epilepsy. Journal of Clinical and Experimental Neuropsychology, 18(5), 747-754.

Sommerbeck, K. W., Theilgaard, A., Rasmussen, K. E., Løhren, V., Gram, L., & Wulff, K. (1977). Valproate sodium: Evaluation of so-called psychotropic effect. A controlled study. Epilepsia, 18(2), 159-167.

Spreen, O., & Strauss, E. (1991). A compendium of neuropsychological tests. New York: Oxford.

Spreen, O., & Strauss, E. (1998). A compendium of neuropsychological tests (2nd ed.). New York: Oxford.

Stevens, J. (1986). Applied multivariate statistics for the social sciences. Hillsdale, NJ: Lawrence Erlbaum Associates.

Stevens, J. R., Milstein, V., & Goldstein, S. (1972). Psychometric test performance in relation to the psychopathology of epilepsy. Archives of General Psychiatry, 26, 532-538.

Strauss, E., Wada, J., & Hunter, M. (1992). Sex-related differences in the cognitive consequences of early left-hemisphere lesions. Journal of Clinical and Experimental Neuropsychology, 14(5), 738-748.

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. Journal of Experimental Psychology, 18, 643-662.

Tabachnik, B.G., & Fidell, L.S. (1996). Using multivariate statistics. 3rd edition. New York: Harper Collins.

Thompson, P. J. (1991). Memory function in patients with epilepsy. Advances in Neurology, 55, 369-384.

Thompson, P. J. (1992). Antiepileptic drugs and memory. Epilepsia, 33(Suppl 6), S37-S40.

Thompson, P. J., & Oxley, J. (1988). Socioeconomic accompaniments of severe epilepsy. Epilepsia, 29(Suppl 1), S9-S18.

Thompson, P. J., & Trimble, M. R. (1981). Further studies on anticonvulsant drugs and seizures. Acta Neurologica Scandinavica, 64(Suppl 89), 51-57.

Thompson, P. J., & Trimble, M. R. (1983). Anticonvulsant serum levels: Relationship to impairments of cognitive functioning. Journal of Neurology, Neurosurgery, and Psychiatry, 46, 227-233.

Thompson, P. J., & Trimble, M. R. (1996). Neuropsychological aspects of epilepsy. In I. Grant & K. M. Adams (Eds.), Neuropsychological assessment of neuropsychiatric disorders (pp. 263-287). New York: Oxford.

Tomlinson, L., Stirling, N., Merryfield, E., & Reynolds, E. H. (1981). Recognition memory in treated epileptic patients. Acta Neurologica Scandinavica, 64(Suppl 89), 43-50.

Trimble, M. R., & Thompson, P. J. (1983). Anticonvulsant drugs, cognitive function, and behavior. Epilepsia, 24(Suppl 1), S55-S63.

Tröster, A. I., Massman, P., Butters, N., Delis, D. C., Economou, V., Iragui, V. J., & Watson, D. P. (1989). Verbal learning and memory in patients with complex partial seizures of temporal lobe origin. Epilepsia, 30(5), 732.

Van Gorp, W. G., Satz, P., Kiersch, M. R., & Henry, R. (1986). Normative data on the Boston Naming Test for a group of normal older adults. Journal of Clinical and Experimental Neuropsychology, 8, 702-205.

Verhoeff, N. P. L. G., Aldenkamp, A. P., Overweg, J., Van Royen, E. A., Verbeeten, B., & Weinstein, H. C. (1992). Memory complaints, memory disorders and focus localization in patients with partial epilepsy. Seizure, 1, 149-156.

Watts, F. N., & Sharrock, R. (1985). Description and measurement of concentration problems in depressed patients. Psychological Medicine, 15, 317-326.

Wechsler, D. (1945). A standardized memory scale for clinical scale use. Journal of Psychology, 19, 87-95.

Wechsler, D. (1987). Wechsler Memory Scale - Revised manual. San Antonio, TX: The Psychological Corporation.

Wiens, A. N., Tindall, A. G., & Crossen, J. R. (1994). California Verbal Learning Test: A normative data study. The Clinical Neuropsychologist, 8(1), 75-90.

Table 1.

Seizure Etiology (Adams & Victor, 1993; Lothman & Collins, 1990).

Acquired or Symptomatic Etiology

- Congenital
  - Maldevelopment
  - Inborn metabolic errors
- Perinatal
  - Immediate: hypoxemia, hemorrhage, trauma
  - Latent: temporal lobe sclerosis
- Metabolic
  - Hypocalcemia
  - Hyponatremia
  - Hypoglycemia
- Infectious
  - Simple febrile convulsions
  - Encephalitis
  - Meningitis
- Neoplastic
  - Primary
  - Metastatic
- Vascular
  - Arteriovenous malformation
  - Postinfarction
  - Posthemorrhage
- Trauma
  - Penetrating wounds
  - Closed head injuries
- Toxins
  - Drug abuse
  - Withdrawal from alcohol and sedative drugs

Idiopathic Etiology

Etiology undetermined, often a heritable tendency.

Table 2.

International Classification of Epileptic Seizures (ICES; Commission on Classification and Terminology of the International League Against Epilepsy, 1981).

I. Partial (or focal) seizures

A. Simple partial seizures. There is no impairment of consciousness. The EEG shows epileptic activity localized in surface leads.

1. With motor signs.
2. With somatosensory or special-sensory symptoms (simple hallucinations, e.g., tingling, light flashes, buzzing).
3. With autonomic symptoms or signs (including epigastric sensation, pallor, sweating, flushing, pilo-erection and pupillary dilatation).
4. With psychic symptoms (disturbance of higher cerebral function). These symptoms rarely occur without impairment of consciousness and are much more commonly experienced as complex partial seizures.

B. Complex partial seizures. Alteration or loss of consciousness present. The EEG shows localized, or bilaterally asymmetrical discharges over temporal, or frontotemporal areas.

1. Beginning as simple partial seizures (e.g., psychic aura) and progressing to impairment of consciousness; with or without simple partial seizure symptoms or automatisms.
2. Impairment of consciousness at onset; with or without simple partial seizure symptoms or automatisms.

C. Secondarily Generalized partial seizures

Simple or complex partial seizures evolving into generalized seizures.

II. Primary Generalized seizures. EEG ictal activity is bilaterally symmetrical and without local onset. Consciousness may be impaired.

A. Nonconvulsive.

1. Absence seizures (petit mal). There is abrupt onset, impairment of consciousness, and little or no convulsive movement, although mild motor signs, autonomic symptoms and/or automatisms may occur.
2. Atypical absence. More varied EEG and clinical features, such a tonic posturing.

B. Convulsive. Bilateral motor convulsions from the start.

1. Myoclonic seizures. Single or repetitive jerks of muscles, usually without loss of consciousness.
2. Clonic seizures. Repetitive clonic contractions (jerks) of the upper and lower extremities.
3. Tonic seizures. Rigid contraction (spasm) of the muscles in the body, especially the upper and lower extremities.
4. Tonic-clonic (grandmal). Loss of consciousness. Tonic phase, usually 10 to 20 seconds, followed by clonic jerks which last approximately 30 seconds.
5. Atonic seizures. Also called drop attacks; loss of consciousness and muscle tone.

III. Unclassified epileptic seizures

This includes, for example, some neonatal seizures.

Table 3.

International Classification of Epilepsies and Epileptic Syndromes (ICE; Commission on Classification and Terminology of the International League Against Epilepsy, 1989)

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1. Localization-related (focal, local, partial) epilepsies and syndromes
   - 1.1 Idiopathic (with age-related onset)
     - Benign childhood epilepsy with centrotemporal spikes
     - Childhood epilepsy with occipital paroxysms
     - Primary reading epilepsy
   - 1.2 Symptomatic
     - Chronic progressive epilepsia partialis continua of childhood
     - Syndromes characterized by seizures with specific modes of precipitation
     - Temporal lobe epilepsies
     - Frontal lobe epilepsies
     - Parietal lobe epilepsies
     - Occiptal lobe epilepsies
   - 1.3 Cryptogenic epilepsy
2. Generalized epilepsies and syndromes
   - 2.1 Idiopathic (with age-related onset)
     - Benign neonatal familial convulsions
     - Benign neonatal convulsions
     - Benign myoclonic epilepsy in infancy
     - Childhood absence epilepsy
     - Juvenile absence epilepsy
     - Juvenile myoclonic epilepsy
     - Epilepsy with grand mal seizures on awakening
     - Other generalized idiopathic epilepsies
     - Epilepsies with seizures precipitated by specific modes of activation
   - 2.2 Cryptogenic or symptomatic (in order of age)
     - West syndrome
     - Lennox-Gastaut syndrome
     - Epilepsy with myoclonic astatic seizures
     - Epilepsy with myoclonic absences

2.3 Symptomatic

2.3.1 Non-specific etiology

- Early myoclonic encephalopathy
- Early infantile epileptic encephalopathy with suppression burst
- Other symptomatic generalized epilepsies not defined above

2.3.2 Specific syndromes

- Epileptic seizures may complicate many disease states. Under this heading are included diseases in which seizures are a presenting or predominant feature.

3. Epilepsies and syndromes undetermined whether focal or generalized

3.1 With both generalized and focal seizures

- Neonatal seizures
- Severe myoclonic epilepsy in infancy
- Epilepsy with continuous spike-waves during slow wave sleep
- Acquired epileptic aphasia
- Other undetermined epilepsies not defined above

3.2 Without unequivocal generalized or focal features. All cases with generalized tonic-clonic seizures in which clinical and EEG findings do not permit classification as clearly generalized or localization related, such as in many cases of sleep-grand mal (GTCS) are considered not to have unequivocal generalized or focal features.

4. Special syndromes

4.1 Situation-related seizures

- Febrile convulsions
- Isolated seizures or isolated status epilepticus
- Seizures occurring only when there is an acute metabolic or toxic event due to factors such as alcohol, drugs, eclampsia, nonketotic hyperglycemia

Table 4.

Anticonvulsant Clinical Efficacy (Ayd, 1995; McIntosh, 1992b)

Generic Name	Brand Name	Generalized Tonic-Clonic	Partial Complex	Generalized Absence
Phenytoin	Dilantin	++	++	-
Carbamazepine	Tegretol	++	++	-
Lamotrigine	Lamictal	++	++	-
Primidone	Mysoline	+	++	-
Gabapentin	Neurontin	+	++	-
Felbamate	Felbatol	-	++	++[30]
Phenobarbital	Luminal	+	+	-
Valproic Acid	Depakote	++	+	++
Diazepam	Valium	++[31]	-	++
Clonazepam	Klonopin	+	-	++
Ethosuximide	Zarontin	-	-	++
Methsuximide	Celontin	-	-	++

[30] Used with atypical absence seizures.

[31] Major use with status epilepticus.

Table 5.

Studies Investigating Seizure Related Variables.

Heading	Description
Author	Mirsky et al., 1960
Criteria	EEG, clinical data
Groups (n)	TL (39), FL (18), G (19), NC (25)
Measures	WMS
Results	WMS MQ related to duration and IQ
Author	Scott et al., 1967
Criteria	EEG, clinical data
Groups (n)	1: High seizure frequency (10), Low seizure frequency (14), NC (16) 2: epileptiform EEG (9), abnormal background EEG (5), normal patient EEG (10), NC EEG (16)
Measures	Visual and tactile problem solving and learning. Recognition of recurring figures and nonsense syllables.
Results	No differences related to seizure frequency, EEG abnormality, duration, or age onset.
Author	Schwartz & Dennerll,1969
Criteria	EEG, clinical data
Groups (n)	GM (129), PM (6), PsyM (22), GM+PsyM (36), GM+PM (9), GM+other (31), other (6).
Measures	Recall of Bender Gestalt figures
Results	Total score: GM+PsyM < GM < GM+other. Suggests PsyM seizures are a crucial component related to poor visual recall.
Author	Rausch et al., 1978
Criteria	interictal depth EEG
Groups (n)	TL (12): total activation (TA), degree of lateralization (DL)
Measures	WMS-MQ
Results	MQ not related to age, duration, sz fq, serum ACD level, or gender.
Author	Làdavas et al., 1979
Criteria	EEG, CT
Groups (n)	LT (24), RT (29), RF (12), LF (10)
Measures	auditory & visuospatial learning (span + 1); 20 words with 10 minute del; ROCFT with 10 minute del; recency judgement of words & pictures.

Results	TLE with > 1 yr duration: greater difference between verbal and visual-spatial learning and recall tests. No diffs for gender or CT lesions.
Author	Brittain, 1980
Criteria	clinical data
Groups (n)	E (157), NC (80)
Measures	Forced Choice Recognition for Words and Faces
Results	Words: E<NC; related to known etiology, duration, sz type Faces: E<NC; related to known etiology, duration, age onset.
Author	Delaney et al., 1980
Criteria	EEG, clinical data, unequivocal
Groups (n)	LT (15), RT (15), FL (15), NC (15)
Measures	WMS/LM imm and del recall; WMS/VR imm and del recall; learning & retention of list of fragmented words; recurring figures.
Results	No correlations with age onset or sz fq. Duration negatively correlated with LMimm, LMdel, VRimm, & recurring figures.
Author	Loiseau et al., 1980
Criteria	clinical data
Groups (n)	E (100), NC (73)
Measures	WMS/VR, RAVLT
Results	No effects due to sz fq, sz type, duration, or ACD.
Author	Loiseau et al., 1982
Criteria	EEG, clinical data
Groups (n)	E (56), NC (50)
Measures	144 memory battery scale (French): short story, series of words, complex figure, series of figures. Scores: registration, learning, retrieval & total.
Results	Overall: E<NC, G=CPS. Duration & sz fq correlated with poor memory. ACDs no effect.
Author	Loiseau et al., 1983
Criteria	EEG
Groups (n)	PG (87), UG (23), PE (43), PC (47), NC (100)
Measures	WMS/VR, RAVLT learning and recognition conditions
Results	Overall: E<NC. Poor RAVLT learning associated with all sz types, early onset, lower sz fq, duration _ 20 yrs. Poor RAVLT recogn associated with adult onset; results for duration and sz fq were mixed. Poor WMS VR associated with PG, bilat spike & wave EEG, adolescent onset; results for sz fq were mixed. No effects for EEG focus or ACD.
Author	Loiseau et al., 1984
Criteria	EEG, clinical data

Groups (n)	E (18) G (9), P (9). Matched controls: E/NC (18), G/NC (9), P/NC (9)
Measures	144 memory battery scale (French)
Results	learning: E<NC, G<G/NC, P=P/NC memory: E<NC, G<G/NC, P=P/NC. Poor memory associated with G.
Author	Dodrill, 1986
Criteria	clinical data
Groups (n)	lifetime fq of sz: low (31), medium (38), high (11), status epilepticus (24)
Measures	WMS / VR and LM subtests
Results	LM: No differences. VR: status epilepticus < medium lifetime fq of sz
Author	Bornstein et al., 1988
Criteria	presurgical
Groups (n)	1: CPS (23), CPG (14), PG (11), NCS (9). 2: focal spike & wave (35), diffuse slowing (8), no abnormality (14).
Measures	WMS-R
Results	Figural recognition: CPG<NCS. Visual PAL I: CPS=CPG<NCS Visual PALII: CPS<NCS. Delayed memory: CPS & CPG<NCS &PG VR % retained: CPS<NCS
Author	Hermann et al., 1988
Criteria	CCTV/EEG (majority presurgical)
Groups (n)	dominant TL (25)
Measures	CVLT
Results	Age at onset, etiology, duration, multiple sz types, age, gender, education, handedness, familial sinistrality, VIQ: all not predictors of mem deficit.
Author	Homan et al., 1989
Criteria	DSPECT
Groups (n)	Hypoperfused: LT (31), RT (20), LF (30), RF (16). Normal: LT (20), RT (30), LF (19), RF (34). Also by etiology, sz type, & ACD.
Measures	WMS: LMimm, LMdel, VRimm, VRdel
Results	No differences due to etiology, sz type, or ACD regimen.
Author	Saykin et al., 1989
Criteria	presurgical
Groups (n)	EO=early onset (< 6 yrs), LO = later onset LT/EO (7), LT/LO (6), RT/EO (6), RT/LO (11)
Measures	WMS: LMimm, LMdel, VRimm, VRdel
Results	overall memory: EO < LO. LT: relative verbal deficit. RT: no difference.
Author	Strauss et al., 1992
Criteria	Wada, CCTV/EEG

Groups (n)	male L speech (ML; 4), male atypical speech (MA; 4), female L speech (FL; 7), female atypical speech (FA; 9)
Measures	WMS: LM imm, LM del, VR imm, VR del
Results	LM imm, VR imm, VR del: FA<FL LM imm & del, VR imm & del: MA=ML Memory below normal: MA, ML, FA. Memory scores normal: FL.
Author	Verhoeff et al., 1992
Criteria	EEG, SPECT, CT
Groups (n)	memory impairment: global (13), verbal (5), figural (5), no problems (5)
Measures	AVLT delayed recall, ROCFT delayed recall
Results	Sz type, frequency, type of epilepsy, age at onset, duration, type ACD: all unrelated to type or severity of memory impairment.
Author	Seidenberg et al., 1993
Criteria	presurgical
Groups (n)	LT (44), RT (47)
Measures	CVLT recognition memory
Results	No correlation between age at onset or gender and verbal recognition memory.
Author	Baxendale et al., 1998
Criteria	presurgical
Groups (n)	LHS (36), RHS (30), no abnormality (13)
Measures	AMIBP (list learning, story recall, design learning, figure recall)
Results	Age at onset helped predict delayed and % retained story recall & immed figure recall. Duration helped predict delayed figure recall.

Table 6.

Studies Investigating Location of Seizure Onset, Non-Surgical Candidates.

Heading	Description
Author	Mirsky et al., 1960
Criteria	EEG, clinical data
Groups (n)	TL (39), FL (18), G (19), NC (25)
Measures	WMS
Results	No differences among groups. MQ related to duration and IQ.
Author	Glowinski, 1973
Criteria	"judged"
Groups (n)	TL (30), G (30), NC (23)
Measures	WMS plus LM del. Half the patients were in divided attention condition.
Results	IQ-MQ: T<G. LM imm: T<G. LM del: both T & G poor verbal PAL: no differences. E affected more by divided attn. TL 'laterality': no differences
Author	Rausch et al., 1978
Criteria	interictal depth EEG
Groups (n)	TL (12). Measured total activation (TA) & degree of lateralization (LAT)
Measures	SRT, WMS with verbal PAL del and VR del
Results	MQ: related to LAT PAL del & (PAL del-VR del) related to LAT max on R side.
Author	Làdavas et al., 1979
Criteria	EEG, CT
Groups (n)	LT (24), RT (29), RF (12), LF (10)
Measures	auditory & visuospatial learning (span + 1); 20 words with 10 minute del; ROCFT with 10 minute del; recency judgement of words & pictures.
Results	Del recall: T<F. Recency: F<T. Learning difference score (verbal-visual): LT<RT (LT negative score, RT positive score). Recall difference score (verbal-visual): LT<RT (LT negative, RT positive). TLE with > 1 yr duration: greater difference between verbal and visual-spatial learning and recall tests.
Author	Delaney et al., 1980
Criteria	EEG, clinical data, unequivocal
Groups (n)	LT (15), RT (15), FL (15), NC (15)

Measures	WMS: LM imm, LM del recall, VR imm VR del; learning & retention of list of fragmented words; recurring figures.
Results	LM imm: TL<FL,NC. LM del: LT< RT, FL, NC VR imm: no diffs. VR del: RT<FL,NC; LT=FL=NC Recurring figures: RT<LT,FL,NC; LT=FL=NC fragmented wds (1) learning & recogn: no diffs (2) free recall: LT<FL, NC
Author	Mayeux et al., 1980
Criteria	EEG
Groups (n)	LT (14), RT (7), G (8)
Measures	WMS (including LM del), BVRT (recognition), ROCFT (20 min delay)
Results	WMS, ROCFT recall, & BVRT: no diffs
Author	Loiseau et al., 1982
Criteria	EEG, clinical data
Groups (n)	E (56), NC (50)
Measures	144 memory battery scale (French)
Results	Overall: E<NC, G=CPS. Unilateral EEG focus associated with poor verbal and visual memory. Bilateral EEG foci associated with verbal and visual memory plus percent retained.
Author	Loiseau et al., 1983
Criteria	EEG
Groups (n)	PG (87), UG (23), PE (43), PC (47), NC (100)
Measures	WMS VR, RAVLT learning and recognition conditions
Results	Overall: E<NC. Poorer WMS VR and RAVLT learning for bilateral spike & wave EEG group. Unilateral frontal or temporal EEG focus groups not different from controls.
Author	Masui et al., 1984
Criteria	EEG, CT
Groups (n)	LT (10), RT (12), NC (15)
Measures	imm and del of 20 words presented on either side of visual field
Results	Correct, Retention: TL<NC LT poor retention for words presented to RVF, but RT no effect.
Author	Mungas et al., 1985
Criteria	EEG
Groups (n)	LT (11), RT (10), NC (11)
Measures	AVLT: 2 words in 8 categories, concrete versus abstract, phonemic & semantic cued recall.
Results	learning, recall: no effects. Greater decline in recall after a delay, and poorer phonemic cued recall, for LTL group.

Author	Tröster et al., 1989
Criteria	CT, EEG, ictal EEG in 75%
Groups (n)	LT (12), RT (8) [matched]
Measures	CVLT
Results	imm free recall, short & long delay recall, discrim & FP errs: LT<RT, NC. free & cued recall: LT, RT < NC. Long delay cued recall: LT < RT.
Author	Andrewes et al., 1990
Criteria	video EEG, depth EEG
Groups (n)	interictal: LT (8), RT (7). postictal: LT (4), RT (4), NC (43)
Measures	Recogn tests: 16 lists of 60 abstract words, 16 lists of 30 abstract "shapes"
Results	No interictal diffs. Interictal vs. postictal: difference scores predict side of focus.
Author	Giovagnoli & Avanzini, 1996
Criteria	ictal EEG, MRI
Groups (n)	LT (43), RT (36), NC (33)
Measures	Buschke SRT
Results	long term retrieval: LT<RT, NC

Table 7.

Studies Investigating Location of Seizure Onset, Epilepsy Surgery Candidates.

Heading	Description
Author	Hermann et al., 1987
Criteria	presurgical
Groups (n)	LT (15), RT (15), NC (15)
Measures	CVLT
Results	verbal learning, imm free recall, retrieval efficiency: LT<RT,NC. Semantic clustering: LT < NC.
Author	Saykin et al., 1989
Criteria	presurgical
Groups (n)	EO=early onset (< 6 yrs), LO= later onset, LT/EO (7), LT/LO (6), RT/EO (6), RT/LO (11)
Measures	WMS: LM imm, LM del, VR imm, VR del
Results	LT: relative verbal deficit. RT: no difference.
Author	Helmstaedter et al., 1991
Criteria	presurgical
Groups (n)	LT (24), RT (19), BiT (34), NC (57)
Measures	visual learning
Results	RT, BiT< LT, NC
Author	Jones-Gotman, 1991
Criteria	presurgical EEG & depth electrodes
Groups (n)	LT uni (15), LT bi (16), RT uni (16), RT bi (28)
Measures	WMS: LM del + verb PAL del (del verbal), VR del (del visual-spatial)
Results	del verbal: LT bi < LT uni < RT bi < RT uni del visual-spatial: RT uni = RT bi = LT bi < LT uni
Author	Christianson et al., 1992
Criteria	presurgical
Groups (n)	1: LT (34), RT (18), NC (20). 2: LT (34),RT (15),NC (20)
Measures	1: word lists. 2: random shapes. Each item presented to one visual field.
Results	1: word recall: LT<NC; LVF<RVF except LT patients and abstract words. 2: visual-spatial recogn: LT, RT < NC. No visual field effects.
Author	Hermann et al., 1992
Criteria	presurgical

Groups (n)	LT (47), RT (52)
Measures	CVLT
Results	After accounting for influence of demographic variables and language function, laterality not a significant predictor of CVLT performance.
Author	Seidenberg et al., 1993
Criteria	pre- and post-surgical
Groups (n)	LT (44), RT (47)
Measures	CVLT (recognition memory indices)
Results	Discriminability index: RT>LT; Response bias, false positives: LT>RT. LT more errors of all types than RT.
Author	McGlone, 1994
Criteria	pre- and post-surgical
Groups (n)	LT (19; 10 M, 9 F), RT (28; 13 M, 15 F)
Measures	WMS, verbal PAL del, ROCFT del
Results	verbal PAL del: RT>LT, female>male. ROCFT del: no overall L vs R effect, but male LT>male RT, male LT>female LT
Author	Helmstaedter et al., 1995
Criteria	presurgical
Groups (n)	LT (30), RT (30), NC (30)
Measures	AVLT, BVRT (immed only)
Results	AVLT learning & BVRT: LT=RT<NC. Short & long del recall: LT<RT=NC. AVLT learning ass'd with BVRT complexity in RT group.
Author	Hermann et al., 1995
Criteria	presurgical, all depth EEG
Groups (n)	LT (48), RT (29)
Measures	WRMT: recognition of faces and names
Results	No differences.
Author	Breier et al., 1996
Criteria	location of surgery
Groups (n)	LT (31), RT (37), ET (17)
Measures	LMI, LMII, verbal SRT with delay, VRI, VRII, ROCFT, non-verbal SRT
Results	VSRT last trial: LT<ET; VSRT delay: no diffs; LMII: LT,RT<ET. NVSRT last trial, ROCFT del, & VRII: RT<ET
Author	O'Shea et al., 1996
Criteria	presurgical
Groups (n)	LT (23), RT (16), PG (38)
Measures	WMS: LM, verbal PAL

Results	LM: LT, RT < PG. PAL: no diffs, but for hard word pairs: LT<RT,PG
Author	Snitz et al., 1996
Criteria	presurgical
Groups (n)	LT (20), RT (17)
Measures	CVMT (acquisition, delayed recognition), WMS-R, RAVLT, ROCFT
Results	CVMT group diffs due to FSIQ not seizure focus. CVMT not rel'd to other measures of visual mem but it is rel'd to many WAIS-R variables.
Author	Thompson & Trimble, 1996
Criteria	presurgical
Groups (n)	LT (14), RT (20)
Measures	list learning, story recall, word recogn, design learning, complex figure, face recogn
Results	No significant LT vs RT diffs. Trends in expected directions.

Table 8.

Studies Investigating Hippocampal Cell Density.

Heading	Description
Author	McMillan et al., 1987
Criteria	surgery, hippocampal sclerosis
Groups (n)	LT/HS (13), RT/HS (11), LT/NoHS (6), RT/NoHS (10)
Measures	WMS: LM imm, LM del; ROCFT
Results	LM imm & LM del: LHS=RHS, LNoHS< RNoHS. LM %retained: No differences. ROCFT del & %retained: No differences.
Author	Sass et al., 1990
Criteria	presurgical, hippocampal cell densities
Groups (n)	LT (17), RT (18)
Measures	Buschke SRT
Results	SRT: TLE<NC, LT<RT. long-term retrieval score correlated with CA3 and hilus cell densities in LT only.
Author	Lencz et al., 1992
Criteria	surgery, MRI hippocampal volume, cell densities
Groups (n)	LT (12), RT (13), NC (14)
Measures	WMS: LM imm, LM del, VR imm, VR del, SRT
Results	SRT: correlated with LT volume and LT-RT ratio. LM % retained: correlated with L hippocampal volume in LTL. No correlations with R hippocampal or RT measures.
Author	Sass et al., 1992
Criteria	presurgical, hippocampal cell count
Groups (n)	LT (28), RT (31)
Measures	WMS: LM imm, LM del
Results	LM: LT<RT. LM % retention correlated with CA3 and hilar areas, but only for LTL.
Author	Miller et al., 1993
Criteria	surgery, hippocampal sclerosis
Groups (n)	LT/HS (13), RT/HS (12), LT/NoHS (10), RT/NoHS (5), NC (10)
Measures	WMS: LM imm, LM del, verbal PAL imm, verbal PAL del, ROCFT, WRMT faces & words.

Results	WRMT, LM imm: no differences. LM del: LHS<NC. ROCFT copy-delay: poorer in HS groups. ROCFT del: trend HS < NoHS, NC, no side of lesion effects. PAL learning+recall: LHS<NC. PAL learning: LHS, RHS, LNoHS < NC
Author	Rausch & Babb, 1993
Criteria	presurgical, hippocampal cell loss
Groups (n)	mild LT (5), severe LT (7), mild RT (7), severe RT (6), NC autopsy (4)
Measures	WMS: LM imm, LM del, VR imm, VR del, verbal PAL imm, verbal PAL del, ROCFT
Results	PAL del: LT<RT. LM del: LT<RT. PAL imm & del: related to cell loss in LT only, and severe LT < mild-mod LT. No visual memory differences.
Author	Saling et al., 1993
Criteria	hippocampal sclerosis
Groups (n)	LHS (20), RHS (18)
Measures	WMS: verbal PAL, LM imm, LM del
Results	PAL: LHS < RHS. No other significant differences.
Author	Baxendale et al., 1994
Criteria	hippocampal volume and hippocampal sclerosis
Groups (n)	(32) TLE patients with HS
Measures	learning, recall, and recognition of verbal and non-verbal material
Results	list learning intrusions, % retained story recall: RHS < LHS design learning: anterior RHS < diffuse RHS naming: diffuse LHS < anterior LHS
Author	Sass et al., 1995
Criteria	hippocampal cell count, lesion
Groups (n)	LT lesion (11), RT lesion (11)
Measures	WMS: LM imm, LM del, LM %retained, Buschke SRT (LTR score)
Results	LTR: LT lesion<RT lesion. Correl's within LT lesion grp: LM imm & LM del; LM %retained & LTR & LM del; FSIQ & LM imm. Correl's between mem scores & cell count areas: CA1 & LTR; CA2 & LM %retained. Correl's within RT lesion group: LM imm & LM del & LTR; LM del & LM %retained & LTR; FSIQ & LM imm & LTR. No correl's with hippocampal cell counts. Results similar to pts without lesions.
Author	Kälviäinen, et al., 1997
Criteria	new diagnosis, unmedicated
Groups (n)	LT (12), NC (15)
Measures	immediate & delayed story recall, word list

Results	L hippocampal volume correlated with immediate & delayed story recall & delayed word list recognition.
Author	Baxendale et al., 1998
Criteria	hippocampal volume and hippocampal sclerosis
Groups (n)	LHS (36), RHS (30), no abnormality (13)
Measures	AMIPB (list learning, story recall, design learning, figure recall)
Results	imm & del story recall: LHS<RHS. L hippocampal volume predicted imm story recall. R hippocampal volume helped predict del figure recall.

Table 9.

Studies Investigating Cerebral Pathology.

Heading	Description
Author	Làdavas et al., 1979
Criteria	EEG, CT
Groups (n)	LT (24), RT (29), RF (12), LF (10)
Measures	auditory & visuospatial learning (span + 1); 20 words with 10 minute del; ROCFT with 10 minute del; recency judgement of words & pictures.
Results	No differences related to CT lesions.
Author	Homan et al., 1989
Criteria	DSPECT
Groups (n)	Hypoperfused: LT (31), RT (20), LF (30), RF (16). Normal: LT (20), RT (30), LF (19), RF (34). Also by etiology, sz type, ACD.
Measures	WMS: LM imm, LM del, VR imm, VR del
Results	LM imm helps predict LT and RF rCBF. LM del not a predictor. VR imm helps predict LF rCBF. VR del helps predict LT, RT rCBF.
Author	Verhoeff et al., 1992
Criteria	EEG, SPECT, CT
Groups (n)	memory impairment: global (13), verbal (5), figural (5), no problems (5)
Measures	AVLT delayed recall, ROCFT delayed recall
Results	Global: associated with PL and FL pathology. Non-global (i.e., verbal or figures): associated with TL pathology. EEG focus not related to type/severity of memory impairment.
Author	Sass et al., 1995
Criteria	hippocampal cell count, lesion
Groups (n)	LT lesion (11), RT lesion (11)
Measures	WMS: LM imm, LM del, LM %retained, Buschke SRT (LTR score)
Results	Results were similar for patients with and without lesions (see Table 8).

Table 10.

Studies Investigating Anticonvulsant Drug Effects.

Heading	Description
Author	Sommerbeck et al., 1977
Criteria	triple blind crossover
Groups (n)	VPA only (13), VPA+clonazapam (7)
Measures	verbal PAL
Results	No effect
Author	Thompson & Trimble, 1981
Criteria	change in ACD
Groups (n)	A: ACD reduced or withdrawn & CBZ added (15), B: ACD reduction only (20), C: no change (10)
Measures	20 pictures and words, immed & delay recall, delay recognition
Results	A: all recall scores improved, sz control improved. B: only delayed picture recall improved.
Author	Thompson & Trimble, 1982
Criteria	change in ACD
Groups (n)	A: change from polytherapy to monotherapy (20), B: ACD reduction & CBZ added (15), C: PB or PRM discontinued (8), D: no change (10)
Measures	20 pictures and words, immed & delay recall, delay recognition
Results	B: memory improved, sz control improved. C: memory improved, sz control declined.
Author	Thompson & Trimble, 1983
Criteria	serum ACD levels
Groups (n)	Various: High serum vs. Low serum (28)
Measures	20 pictures and words, immed & delay recall, delay recognition
Results	pictures & words, immed recall; attn, mental speed: high< low serum
Author	Trimble & Thompson, 1983
Criteria	monotherapy serum ACD level
Groups (n)	PT (9), VPA (7), CBZ (8)
Measures	20 pictures and words, immed & delay recall, delay recognition
Results	Within PT & VPA groups: poorer imm recall of pictures (and poorer attn & mental speed) associated with high serum level. Within CBZ group: no memory effect (but poorer attn & motor speed at high serum level).

Author	Andrewes et al., 1984
Criteria	new referrals
Groups (n)	CBZ (16), PT (16)
Measures	word list learning, forgetting, & re-learning; prose recall (immed, delay; cued); picture recognition
Results	no effects
Author	Ludgate et al., 1985
Criteria	reduce polytherapy
Groups (n)	E (12) polytherapy changed to monotherapy
Measures	BVRT (details regarding format not provided)
Results	Fewer errors on BVRT after change to monotherapy. Change in sz frequency not a factor.
Author	Andrewes et al., 1986
Criteria	monotherapy, serum ACD level
Groups (n)	CBZ (21), PT (63), no therapy (21)
Measures	word list learning, prose recall
Results	Delayed cued prose recall, list learning (relearning): CBZ > PT, no therapy. Serum level had no effect.
Author	Gallassi et al., 1986
Criteria	seizure free, monotherapy
Groups (n)	PB (9), CBZ (7) controlled withdrawal
Measures	verbal and spatial learning (supraspan: #trials to learn span + 2)
Results	No between or within group effects.
Author	Gallassi et al., 1987
Criteria	seizure free, monotherapy
Groups (n)	PHT (10), NC (10) controlled withdrawal
Measures	verbal and spatial learning (supraspan: # trials to learn span + 2)
Results	No between or within group effects.
Author	Gallassi et al., 1988
Criteria	seizure free, monotherapy
Groups (n)	CBZ (13), PT (12), NC (26) controlled withdrawal
Measures	verbal and spatial learning (supraspan: # trials to learn span + 2)
Results	No between group effect; no within group analyses.
Author	Prevey et al., 1989
Criteria	uncontrolled idiopathic epilepsy
Groups (n)	E (8) polytherapy changed to VPA monotherapy
Measures	ROCFT, RAVLT (standard immed and delay recall)

Results	No effect
Author	Meador et al., 1990
Criteria	double-blind, triple crossover
Groups (n)	E (15) / CBZ, PB, PHT
Measures	SRT
Results	No between group effect.
Author	Durwen et al., 1992
Criteria	presurgical
Groups (n)	LT (13) / Full vs. Reduced ACD
Measures	AVLT
Results	Short delay recall: full < reduced. Trial 5-short delay: reduced< full.
Author	Gallassi, et al., 1992
Criteria	seizure free, monotherapy
Groups (n)	PB (27), CBZ (18), PHT (16), VPA (29), NC (28) controlled withdrawal
Measures	verbal and spatial learning (supraspan: # trials to learn span + 2)
Results	No between or within subject effects.
Author	Durwen et al., 1993
Criteria	presurgical
Groups (n)	LT (13), RT (14) / Full vs. Reduced
Measures	AVLT
Results	Group effects for LT but not for RT. Short delay recall: full < reduced; trial 5-short delay: reduced< full.
Author	Pulliainen & Jokelainen, 1994
Criteria	newly diagnosed, randomly assigned
Groups (n)	PHT (20), CBZ (23), NC (21) / before vs. after starting therapy
Measures	serial digit learning (9 digits), visuospatial learning (7 blocks), BVRT immed & delay, RMT for words and faces.
Results	PHT: Absence of practice effect on BVRT.

Table 11.

Studies Investigating Cognitive Correlates of Memory Performance

Heading	Description
Author	Mirsky et al., 1960
Criteria	EEG, clinical data
Groups (n)	TL (39), FL (18), G (19), NC (25)
Measures	WMS, continuous performance test (CPT)
Results	WMS: no effect. CPT: G < TL, FL.
Author	Schwartz & Dennerll, 1969
Criteria	EEG, clinical data
Groups (n)	GM (129), PM (6), PsyM (22), GM+PsyM (36), GM+PM (9), GM+other (31), other (6).
Measures	Recall of Bender Gestalt figures
Results	IQ not related to visual-spatial mem in group with a mem deficit (i.e., GM+PsyM). IQ related to visual-spatial mem in the remaining groups.
Author	Mayeux et al., 1980
Criteria	EEG
Groups (n)	LT (14), RT (7), G (8)
Measures	WMS (including LM del), BVRT, ROCFT, auditory and visual consonant trigrams, BNT, COWA
Results	COWA and most mem tests: no diffs. BNT: LT < RT, G. LT related to poor naming, but no memory deficits in this group of volunteers. BNT correlated with LM imm, MQ, auditory trigrams (9 sec), & COWA.
Author	Tomlinson et al., 1981
Criteria	EEG, CT, clinical data,
Groups (n)	E (12), NC (12)
Measures	Words presented 4, 2, or 1 time(s). 10 min delay recognition.
Results	Difference in number of words recognized due to Verbal IQ not epilepsy.
Author	Loiseau et al., 1984
Criteria	EEG, clinical data
Groups (n)	E (18) G (9), P (9). Matched controls: E/NC (18), G/NC (9), P/NC (9)

Measures	144 memory battery scale, Raven's Progressive Matrices, six attention tests: (1) count backward & forward, (2) classify circles according to size & cross out a particular figure among others in an array, (3) count words beginning with a particular letter within a story, (4) cross out particular sequences of black & white shapes among others in an array, (5) repeat a series of digits backward, (6) immed recall of spatial location of blocks.
Results	Attention and IQ not related to memory scores in epilepsy patients.
Author	Powell et al., 1984
Criteria	presurgical
Groups (n)	TL (20), hospitalized neurotic (20), NC (20)
Measures	10 lists of 10 words, immediate recall
Results	Strategy noted in which patients rehearsed earlier items at expense of later ones.
Author	Ludgate et al., 1985
Criteria	reduction in polytherapy
Groups (n)	E (12) polytherapy changed to monotherapy
Measures	BVRT (details regarding format not provided), IQ, concentration.
Results	Fewer errors on BVRT after change to monotherapy. Change in sz frequency not a factor.
Author	Dodrill, 1986
Criteria	clinical data
Groups (n)	lifetime fq of sz: low (31), medium (38), high (11), status epilepticus (24)
Measures	WMS: VR and LM subtests, Stroop, TMT-B, WAIS
Results	Compare to norms: Stroop scores high, mem largely unimpaired, TMT-B borderline, Digit Symbol & Arithmetic low in high frequency group. No correlations between IQ and memory.
Author	Hermann et al., 1988
Criteria	CCTV/EEG (majority presurgical)
Groups (n)	dominant TL (25)
Measures	CVLT, MAE
Results	Best predictors of CVLT performance: visual naming, COWA. VIQ not a predictor of memory deficit.
Author	Prevey et al., 1988
Criteria	unequivocal EEG & other diagnostic tests
Groups (n)	LT (13), RT (13), NC (13)
Measures	Estimate verbal and visual memory span and test verbal and visual memory span. Feeling of knowing.

Results	LT poor at predicting verbal span & RT poor at predicting visual span (no statistical comparison). TLE tend to overestimate memory capacities.
Author	Helmstaedter et al., 1991
Criteria	presurgical
Groups (n)	LT (24), RT (19), BiT (34), NC (57)
Measures	visual learning, letter cancellation, block design
Results	Attention not related to visual memory. Attention worst for BiT group.
Author	Hermann et al., 1992
Criteria	presurgical
Groups (n)	LT (47), RT (52)
Measures	CVLT, MAE
Results	Age, gender, education correlated with 4/6 CVLT indices. Language functioning associated with 3/6 CVLT indices. After accounting for influence of demographic variables and language function, laterality not a significant predictor for CVLT performance.
Author	Sass et al., 1992
Criteria	presurgical
Groups (n)	LT (28), RT (31)
Measures	LM imm, LM del, BNT, Verbal WAIS-R IQ
Results	VIQ: LT=RT. LM imm, LM del, LM %retained, BNT: LT < RT. LM imm & LM del both correlated with BNT & VIQ (except LM del not correlated with BNT in RT), but LM %retained not correlated with BNT or VIQ.
Author	Seidenberg et al., 1993
Criteria	pre- and post-surgical
Groups (n)	LT (44), RT (47)
Measures	CVLT (recognition memory indices)
Results	Discriminability index: RT > LT. Response bias, false positives: LT>RT. LT more errors of all types than RT. No correlation between IQ & mem.
Author	Helmstaedter et al., 1995
Criteria	presurgical
Groups (n)	LT (30), RT (30), NC (30)
Measures	AVLT, BVRT (immed only), letter cancellation, vocabulary test
Results	letter cancellation: LT=RT<NC. In RT group: AVLT learning associated with BVRT complexity. Differences in attn do not account for results.
Author	Sass et al., 1995
Criteria	hippocampal cell count, lesion
Groups (n)	LT lesion (11), RT lesion (11)
Measures	WMS: LM imm, LM del, LM %retained, Buschke SRT (LTR score)

Results	IQ not related to verbal mem in the group with a mem deficit (i.e., LT). IQ related to verbal mem in the group without a mem deficit (i.e., RT).
Author	Breier et al., 1996
Criteria	location of surgery
Groups (n)	LT (31), RT (37), ET (17)
Measures	LMI, LMII, verbal SRT with delay, VRI, VRII, ROCFT, non-verbal SRT
Results	VSRT del: only measure on which ET<TL -- note that retrieval strategy not supplied.
Author	Giovagnoli & Avanzini, 1996
Criteria	ictal EEG, MRI
Groups (n)	LT (43), RT (36), NC (33)
Measures	VDMT (Peterson paradigm with words), Buschke SRT, WCST, word fluency
Results	LT: VDMT associated with short term storage and long term retrieval. RT: VDMT associated with short term storage.
Author	Thompson & Trimble, 1996
Criteria	presurgical
Groups (n)	LT (14), RT (20)
Measures	list learning, story recall, word recognition, design learning, complex figure, face recognition
Results	No correlation between IQ and memory.

Table 12.

Studies Investigating Psychosocial Correlates of Memory Performance.

Heading	Description
Author	Stevens et al., 1972
Criteria	EEG, clinical data
Groups (n)	TL (29), G (14), FL (6)
Measures	WMS, WAIS, HRB, MMPI
Results	MMPI: No group differences, highest scale 8. WMS: No group differences. MMPI correlations with test scores: largely non-significant.
Author	Loiseau et al., 1980
Criteria	clinical data
Groups (n)	E (100), NC (73)
Measures	WMS: VR subtest, RAVLT
Results	VR: E < NC for intellectuals & students. RAVLT learning: E < NC for students. RAVLT recogn: E < NC for intellectuals.
Author	Loiseau et al., 1982
Criteria	EEG, clinical data
Groups (n)	E (56), NC (50)
Measures	144 memory battery scale
Results	Education & age contribute to total memory.
Author	Dodrill & Batzel, 1986
Criteria	All patients on record
Groups (n)	E (833)
Measures	Neuropsychology Battery for Epilepsy (NBE; Dodrill, 1978), MMPI
Results	correlation between % abnormal scores on NBE & MMPI averaage elevation: r = .18
Author	Strauss et al., 1992
Criteria	Wada, CCTV/EEG
Groups (n)	male L speech (ML; 4), male atypical speech (MA; 4), female L speech (FL; 7), female atypical speech (FA; 9)
Measures	WMS: LM imm, LM del, VR imm, VR del
Results	LM imm, VR imm, VR del: FA < FL. LM imm & del, VR imm&del: MA=ML. memory below normal: MA, ML, FA.
Author	Corcoran & Thompson, 1993

Criteria	E: postal questionnaire
Groups (n)	memory complainers (C; 30) non-complainers (NC; 30)
Measures	AMIPB: story recall, list and design learning; BVRT; recogn mem test; belonging test from RBMT, RPM, WCST, BNT, BDI, HAD.
Results	Duration, sz frequency, multiple sz types, location of focus, CPS, # of ACDs: No differences. Story recall imm & del, design learning recall: C < NC. Depression & anxiety: C > NC. C with older onset associated with mood problems.
Author	Seidenberg et al., 1993
Criteria	presurgical
Groups (n)	LT (44), RT (47)
Measures	CVLT recognition memory
Results	No correlation between gender and verbal recognition memory.
Author	McGlone, 1994
Criteria	pre-& post-surgery
Groups (n)	LT (19; 10 M, 9 F), RT (28; 13 M, 15 F)
Measures	WMS, verbal PAL del, ROCFT del recall
Results	verbal PAL: female > male. ROCFT: male LT > male RT, male LT >female LT
Author	Perrine et al., 1995
Criteria	304 E from 25 epilepsy centers.
Groups (n)	very frequent szs (10%), frequent (45%), occasional (38%), no sz in past year (7%)
Measures	LMI, LMII, RAVLT, ROCFT, neuropsychological test battery, QOLIE-89, POMS.
Results	Verbal mem correl'd with attn, mem, & health discouragement scales. Visuospatial mem no correl'n with QOLIE-89 scales. Verbal mem explained 3.6% of Q of L variance. Mood and NP tests both related to self-report of cognitive functioning, but mood more strongly related.

Table 13.

Some Psychosocial Problems Associated with Epilepsy (reviewed by Levin, Banks, & Berg, 1988; reproduced from Hermann & Whitman, 1991).

Family background and adjustment	Overprotection; rejection; overindulgence; alterations in family activities and interactions; decreased parental expectations; poor compliance with medical management; familial maladjustment; increased stress, guilt, and concealment; jealousy in siblings.
Emotional adjustment	Anxiety; depression; low self-esteem; anger; violence; increased psychiatric distress; suicide; psychosis; schizophrenia-like illness; personality change; sexual dysfunction; hysteria; paranoia; epileptic personality; stress; mood disorders; manic states; fear
Interpersonal adjustment	Low marital rates; social isolation; social withdrawal; adverse reactions of others to epilepsy; attitudes of others toward the person with epilepsy
Vocational adjustment	Unemployment; underemployment; employment discrimination; unhappiness with vocational situation
Financial status	Lowered income; dependence on federal subsidy; financial burdens of epilepsy
Adjustment to seizures	Perceived and/or real stigma and discrimination; fear of seizures; lack of understanding of epilepsy; nonacceptance of epilepsy by patient; nondisclosure; embarrassment; dread of seizure occurrence
Medicine and medical management	Patient and physician relationship; physician's knowledge of epilepsy and ability to communicate; compliance with treatment program

Table 14.

Demographic, Neuropsychological, and Neurobiological Characteristics by Patient Group.

Variable[32]		LTL	RTL	BTL	NT/U	NS
Demographic and Predictor Variables						
Years of Age	median:	32	35	41	35	36.5
	M, SD	34.1, 10.1	35.3, 10.4	38.3, 7.8	34.2, 9.5	38.3, 8.8
Years of Education	median:	12	12	13	12	13
	M, SD	13.1, 2.3	13.1, 2.2	13.4, 2.0	12.8, 1.8	13.3, 2.1
Age at Onset Epil'sy	median:	11	15	21	14	17
	M, SD	12.6, 11.1	17.8, 13.1	18.7, 13.3	15.8, 10.1	21.2, 13.1
Duration (in years)	median:	21	18	20	13	14.5
	M, SD	21.4, 12.5	17.8, 11.5	19.6, 11.4	18.5, 11.3	16.0, 9.8
Seizure Frequency	median:	6	8	7.3	8	2
(previous month)	M, SD	11.6, 14.8	16.6, 20.2	9.7, 10.3	12.7, 19	7.2, 13.0
Prorated Full Scale	median:	89	95	91	85	95.5
IQ[33]	M, SD	91.8, 15.5	94.7, 11.9	88.2, 8.3	88.0, 9.6	97.1, 11.8
Boston Naming Test	median:	48	50	47	49	53.5
	M, SD	43.4, 11.6	48.8, 7.0	45.5, 9.6	43.3, 12.0	49.8, 9.8
MMPI-2 Scale 2	median:	59	59	65	64	75
(depression)	M, SD	61.6, 12.0	62.6, 13.4	67.0, 14.9	62.8, 13.6	72.1, 12.4
MMPI-2 Scale 7	median:	55	57	62	64	64
(psychasthenia)	M, SD	56.2, 11.6	60.1, 12.1	63.6, 11.8	60.5, 11.7	62.3, 14.4

[32] The distributions of age at onset (skewness = .7972, $z = 3.90$, $p < .001$) and seizure frequency (skewness = 2.16, $z = 10.34$, $p < .001$) were positively skewed, and the mode (i.e., 42.4% of participants) for years of education was 12. Boston Naming Test (skewness = -1.16, $z = -5.67$, $p < .001$), RAVLT Discriminability (skewness = -.78, $z = -3.70$, $p < .001$), RI index (skewness = -.79, $z = -3.78$, $p < .001$), and VRI raw (skewness = -.90, $z = -4.40$, $p < .001$) scores were negatively skewed.

[33] Prorated FSIQ based on the Vocabulary and Block Design subtests of the Wechsler Adult Intelligence Scale - Revised (Silverstein, 1982).

Table 14 (continued)

Variable		LTL	RTL	BTL	NT	NS
Memory Test Scores						
LM I raw score	median:	22	23	20	24	23
	M, SD	20.1, 8.4	22.8, 7.1	20.5, 7.5	24.5, 7.1	23.3, 6.2
LM II raw score	median:	13	19	14	18	18
	M, SD	14.0, 8.5	17.1, 7.7	14.7, 7.8	18.2, 7.0	18.6, 7.5
RAVLT Long Delay	median:	8	8	6	10	9
	M, SD	7.1, 3.9	8.7, 4.0	6.9, 4.4	9.8, 3.5	8.9, 3.9
RAVLT RI Effect	median:	78.6	84.6	70.3	84	80.6
	M, SD	72.7, 22.2	83.4, 17.4	71.8, 23.9	76.0, 19.7	78.3, 20.0
RAVLT Discriminability	median:	88	92	73	94	94
	M, SD	86.0, 10.7	89.5, 8.7	76.5, 14.6	92.7, 8.1	91.5, 8.4
VR I raw score	median:	34	32	29	32	35
	M, SD	31.2, 7.5	31.5, 6.1	30.6, 5.0	31.2, 4.2	32.9, 6.0
VRII raw score	median:	24	24	18	25	31
	M, SD	22.2, 11.1	22.5, 10.2	19.0, 10.3	23.2, 10.3	27.0, 8.9
Rey-Osterreith CFT Delayed Recall	median:	17	14.5	10	16	15.5
	M, SD	16.0, 7.2	14.6, 8.2	11.4, 7.0	16.4, 7.3	15.4, 5.8
Recurring Figures Discriminability	median:	78.6	74.3	72.9	72.9	75.7
	M, SD	76.1, 12.5	73.0, 10.9	70.7, 10.0	69.1, 10.4	77.5, 10.4

Table 14 (continued)

Variable	LTL	RTL	BTL	NT/U	NS
	n=47	n=49	n=17	n=13	n=16
Frequencies (percentage)					
White	85.1	91.7	70.6	92.3	93.8
Female	53.2	59.2	70.6	61.5	62.5
Full Time Employed	46.7	43.8	18.8	38.5	40.0
Married	40.4	44.9	41.2	30.8	43.8
Right Handed	83.0	79.6	88.2	76.9	93.8
Left-hemisphere Language[34]	77.4	85.3	83.3	75.0	100.0
Idiopathic Etiology	44.7	31.3	29.4	16.7	46.7
Structural Lesion[35] Present	15.2	16.3	0.0	7.7	14.3
Tested as Inpatient	34.0	44.9	29.4	38.5	12.5
Later underwent surgery[36]	78.7	83.7	0.0	7.7	0.0
Number of Anticonvulsant Drugs					
1	19.6	24.5	29.4	23.1	56.3
2	58.7	51.0	35.3	30.8	25.0
3	21.7	20.4	35.3	38.5	18.8

[34] Data regarding language dominance were available for 31 LTL patients, 34 RTL patients, 6 BTL patients, 4 NT/U patients, and 1 NS patient.

[35] i.e., tumour or cyst.

[36] In four cases, surgery was offered but the patient declined.

Table 15.

Descriptive Statistics of The Epilepsy Patients Regarding the T Scores of Six Memory Tests.

			Below 5th Percentile	
Memory Test	Mean	Std.Deviation	Count/N	Percent
T-LMI	45.18	9.88	24 /142	16.9 %
T-LMII	43.53	9.44	28 /142	19.7
T-RAVLT-LD	37.58	16.95	49 /134[37]	36.6
T-VRI	48.20	11.82	18 /142	12.7
T-VRII	40.07	14.80	46 /141	32.6
T-ROCFT-Delay	33.05	16.89	68 /140	48.6

[37] Data missing on eight patients because a different word list learning test was introduced to the test battery.

Table 16.

Results of Principal Components Analysis with Seven Memory Measures.

Memory Measure	Component 1	Component 2
Logical Memory II	**.568**	.467
RAVLT - LD	**.861**	.185
RI Index	**.828**	.091
RAVLT Discriminability	**.786**	.224
Visual Reproduction II	.339	**.740**
Rey-Osterreith CFT - Delayed Recall	.183	**.798**
Recurring Figures Discriminability	.053	**.714**
Percent Variance	48.6	16.0

Table 17.

Descriptive Statisitics of the Verbal and Visual-Spatial Memory Components by Patient Group.

Patient Group	Mean	Std.Dev.	N
Verbal Memory			
LTL	46.88	10.07	47
RTL	52.90	8.58	49
BTL	45.50	10.68	17
NT	53.72	9.86	13
NS	52.04	9.83	16
Visual-Spatial Memory			
LTL	51.80	11.70	47
RTL	48.69	10.05	49
BTL	46.45	7.19	17
NT	49.13	7.39	13
NS	53.21	7.52	16

Table 18.

Correlation Matrix of Predictor Variables.

	Age	Educ'n	Duration	BNT	Scale 2	Scale 7	Verbal Memory	Visual-Sp Memory
L / R TL Focus	.06	.09	-.15	.27**	.04	.15	.31***	-.14
Age		.03	.34***	.09	.37***	.27*	-.03	-.20**
Education			-.18*	.32***	.03	-.02	.05	.10
Duration				-.08	.10	.11	.04	-.19*
BNT					-.04	-.06	.21**	.40***
Scale 2						.74***	-.02	-.22**
Scale 7							-.01	-.29***
Verbal Memory								.00

*** $p \leq .001$, ** $p < .01$, * $p < .03$

Table 19.

Standard Multiple Regression of Predictor Variables on Verbal Memory Component.

Variables	r (with Verbal Mem)	B	β	sr^2 (unique)
BNT	.21**	.271**	.233	.05
Duration	.04	.122	.137	
Age	-.03	-.141	-.134	
Scale 2	-.02	.020	-.025	
Scale 7	-.01	.009	.011	
Education	.05	.046	.002	
R^2 =	.07§	Intercept = 37.97		
Adjusted R^2 =	.02			
R =	.27, p = .25			

** $p < .01$, * $p < .05$

§ Unique variability = .05; shared variability = .02.

Table 20.

Standard Multiple Regression of Predictor Variables on Visual-Spatial Memory Component.

Variables	r (with Vis-Sp Mem)	B	β	sr^2 (unique)
BNT	.40***	.334**	.322	.09
Scale 7	-.29***	-.185*	-.261	.03
Age	-.20**	-.217	-.231	.04
Education	.10	-1.931	-.105	
Duration	-.19*	-.066	-.082	
Scale 2	-.22**	.040	.056	
R^2 =	.24§	Intercept = 53.99		
Adjusted R^2 =	.19			
R =	.49, p < .001			

*** p _ .001,** p < .01, * p < .05

§ Unique variability = .16; shared variability = .08

Table 21.

Number of Persons in Each Patient Group Obtaining a Particular Pattern of Memory Component Test Scores.

Patient Group	Verbal > Vis-Sp	Vis-Sp > Verbal	Verbal = Vis-Sp	Total
LTL	12	25	10	47
RTL	24	12	13	49
BTL	3	6	8	17
Total	39	43	31	113

Table 22.

Number of Persons in Each Patient Group Obtaining a Particular Pattern of Memory Component Test Scores: Patients with Left Hemisphere Speech Dominance Only.

Patient Group	Verbal > Vis-Sp	Vis-Sp > Verbal	Verbal = Vis-Sp	Total
LTL	6	14	4	24
RTL	14	9	6	29
BTL	1	0	4	5
Total	21	23	14	58

Table 23.

Sequential Regressions of (1) Left or Right Unilateral Temporal Lobe Focus, (2) Predictor Variable, and (3) Interaction Between (1) and (2).

I. Dependent Variable: Verbal Memory Component

Variables	r	B	β	sr^2 (incremental)	F Change df(2,92; 3,91)	F Change p value
(1) L/R Focus	.31**	-2.15	-.11	.093		
(2) BNT	.18	.06	.06	.010	1.003	.319
(3) BNT x L/R Focus	.32**	.16	.41	.005	.481	.490

Constant = 44.33

Regression line when LTL = 44.33 + .06 (BNT)

Regression line when RTL = (44.33 - 2.15) + (.06 + .16)(BNT) = 42.18 + .22(BNT)

R^2 = .11

Adjusted R^2 = .08

R = .33, p = .016

Variables	r	B	β	sr^2 (incremental)	F Change df(2,93; 3,92)	F Change p value
(1) L/R Focus	.31**	7.64	.39	.096		
(2) Duration	.02	.10	.12	.006	.619	.434
(3) Dur'n x L/R Focus	.24*	-.07	-.09	.002	.198	.658

Constant = 44.81

Regression line when LTL = 44.81 + .10 (Duration)

Regression line when RTL = (44.81 + 7.64) + (.10 -.07)(Dur'n) = 52.45 + .03 (Dur'n)

R^2 = .10

Adjusted R^2 = .09

R = .31, p = .002

Table 23 (continued).

Sequential Regressions of (1) Left or Right Unilateral Temporal Lobe Focus, (2) Predictor Variable, and (3) Interaction Between (1) and (2).

I. Dependent Variable: Verbal Memory Component

Variables	r	B	β	sr^2 (incremental)	F Change df(2,71; 3,70)	F Change p value
(1) L/R Focus	.31**	29.20	1.48	.164		
(2) Scale 2	.06	.24	.31	.002	.140	.709
(3) Scale2 x L/R Focus	.30**	-.34	-1.14	.046	4.10	.047
Constant = 30.69						

Regression line when LTL = 30.69 + .24(Scale 2)

Regression line when RTL = (30.69 + 29.42) + (.24 - .34)(Scale 2) = 60.11 - .10(Scale2)

R^2 = .21

Adjusted R^2 = .18

R = .46, p = .001

Variables	r	B	β	sr^2 (incremental)	F Change df(2,71; 3,70)	F Change p value
(1) L/R Focus	.31**	21.36	1.08	.164		
(2) Scale 7	.11	.17	.20	.002	.133	.717
(3) Scale7 x L/R Focus	.31**	-.23	-.74	.019	1.625	.207
Constant = 36.11						

Regression line when LTL = 36.11 + .17 (Scale 7)

Regression line when RTL = (36.11 + 21.36) + (.17 -.23)(Scale7) = 57.47 - .06(Scale7)

R^2 = .18

Adjusted R^2 = .15

R = .43, p = .003

Table 23 (continued).

Sequential Regressions of (1) Left or Right Unilateral Temporal Lobe Focus, (2) Predictor Variable, and (3) Interaction Between (1) and (2).

II. Dependent Variable: Visual-Spatial Memory Component

Variables	r	B	β	sr^2 (incremental)	F Change df(2,92; 3,91)	F Change p value
(1) L/R Focus	-.14	-7.10	-.32	.019		
(2) BNT	.47**	.60	.54	.274	35.628	.000
(3) BNT x L/R Focus	-.08	-.02	.04	<.001	.005	.942
Constant = 25.71						

Regression line when LTL = 25.71 + .60 (BNT)

Regression line when RTL = (25.71 - 7.10) + (.60 - .02)(BNT) = 18.61 - .58 (BNT)

R^2 = .29

Adjusted R^2 = .27

R = .54, p = .000

Variables	r	B	β	sr^2 (incremental)	F Change df(2,93; 3,92)	F Change p value
(1) L/R Focus	-.14	-2.54	-.12	.020		
(2) Duration	-.25*	-.21	-.23	.073	7.507	.007*
(3) Dur'n x L/R Focus	-.25*	-.07	-.08	.002	.168	.683
Constant = 56.35						

Regression line when LTL = 56.35 -.21 (Duration)

Regression line when RTL = (56.35 - 2.54) - (.21 + .07)(Dur'n) = 53.81 - .28(Dur'n)

R^2 = .10

Adjusted R^2 = .07

R = .31, p = .026

* The effect of duration became marginal (β = -.25, p < .03) when age was also included in the analysis.

Table 23 (continued).

Sequential Regressions of (1) Left or Right Unilateral Temporal Lobe Focus, (2) Predictor Variable, and (3) Interaction Between (1) and (2).

II. Dependent Variable: Visual-Spatial Memory Component

Variables	r	B	β	sr^2 (incremental)	F Change df(2,71; 3,70)	F Change p value
(1) L/R Focus	-.14	-7.18	-.37	.095		
(2) Scale 2	-.15	-.12	-.15	.018	1.43	.236
(3) Scale2 x L/R Focus	-.11	.02	.07	<.001	.014	.907
Constant = 62.90						

Regression line when LTL = 62.90 - .12 (Scale 2)

Regression line when RTL = (62.90 - 7.18) + (-.12 + .02)(Scale2) = 55.72 - .10(Scale2)

R^2 = .11

Adjusted R^2 = .08

R = .34, p = .037

Variables	r	B	β	sr^2 (incremental)	F Change df(2,71; 3,70)	F Change p value
(1) L/R Focus	-.14	-1.23	-.06	.095		
(2) Scale 7	-.29*	-.19	-.23	.075	6.458	.013
(3) Scale7 x L/R Focus	-.14	-.07	-.22	.002	.137	.712
Constant = 66.38						

Regression line when LTL = 66.38 - .19 (Scale 7)

Regression line when RTL = (66.38 - 1.23) - (.19 + .07)(Scale7) = 65.15 - .26(Scale7)

R^2 = .17

Adjusted R^2 = .14

R = .41, p = .004

Table 24.

Standard Multiple Regression Analysis of Age and Duration on Visual-Spatial Memory Component Using Only Unilateral TL Sample.

Variables	r (with Vis-Sp Mem)	B	β	sr^2 (unique)
Duration	-.25**	-.188*	-.211	.04
Age	-.17	-.095	-.089	
R^2 =	.07§	Intercept = 57.21		
Adjusted R^2 =	.05			
R =	.26, $p < .04$			

** $p < .03$, * $p = .06$

§ Unique variability = .04; shared variability = .03

Table 25.

Standard Multiple Regression Analysis of Age and Duration on Visual-Spatial Memory Component Using Entire Epilepsy Sample.

Variables	r (with Vis-Sp Mem)	B	β	sr^2 (unique)
Age	-.20***	-.171*	-.165	.02
Duration	-.19**	-.115	-.136	
R^2 =	.06§	Intercept = 58.22		
Adjusted R^2 =	.05			
R =	.25, $p < .02$			

*** $p < .01$, ** $p < .03$, * $p = .06$

§ Unique variability = .02; shared variability = .04

Table 26.

Correlation Matrix of Age with the Delayed Memory Tests.

	LMII	RAVLT-LD	RAVLT-RI	RAVLT-Discrim	VRII	ROCFT-D	RF-Discrim
Age	-.04	-.03	-.07	-.08	-.25**	-.18*	-.08

** $p < .01$, * $p < .05$ two-tailed

Table 27.

Results of Principal Components Analysis Using Measures Analogous to Sewell et al. (1988)

Memory Measure	Component 1	Component 2
BNT	**.823**	.159
LM I	**.736**	.389
LM II	**.673**	.472
VR I	.303	**.831**
VR II	.154	**.919**
WAIS-R Vocabulary subtest	**.849**	.089
WMS-R Information/Orientation subtest	**.513**	.222
Percent Variance	53.7	14.4

Table 28.

Results of Principal Components Analysis Including BNT with the Seven Memory Measures Employed in The Present Study.

Memory Measure	Component 1	Component 2
BNT	.071	**.700**
LM II	.499	.578
RAVLT-LD	**.869**	.184
RAVLT-RI	**.834**	.098
RAVLT-Discrim	**.782**	.246
VR II	.345	**.691**
ROCFT-D	.194	**.740**
RF-Discrim	.080	**.633**
Percent Variance	45.3	15.1

Table 29.

Principal Components Analysis Including BNT and Nine Memory Measures.

Memory Measure	Component 1	Component 2	Component 3
BNT	.283	-.001	**.717**
LMI	.185	.222	**.889**
LMII	.211	.397	**.814**
RAVLT - LD	.177	**.869**	.191
RAVLT - RI	.138	**.843**	.075
RAVLT - Discrim	.193	**.779**	.196
VRI	**.824**	.065	.355
VRII	**.771**	.286	.224
ROCFT - D	**.744**	.177	.233
RF - Discrim	**.657**	.120	.052
Percent Variance	46.4	14.7	10.9

Table 30.

Correlations Between BNT and Nine Memory Measures.

	LMI	LMII	RAV'-LD	RAV'-RI	RAV'-Discrim	VRI	VRII	ROCFT-D	RF-Discrim
BNT	.52**	.49**	.20*	.16	.27**	.45**	.33**	.34**	.26**

** $p < .01$, * $p < .05$

Table 31.

Questions for Future Research.

1. Which characteristics of mood disturbance are related to which specific aspects of memory and cognitive functioning? For example, is excessive mind-wandering specifically disruptive to processing and remembering novel information?
2. How do the specific neurophysiological changes due to seizures affect cognitive functioning?
3. How sensitive is Scale 7 of the MMPI-2 to diffuse cerebral dysfunction?
4. Why was the effect of age, but not duration, a significant predictor of visual-spatial memory component score when the entire epilepsy sample was considered, whereas duration, but not age, was a marginally significant predictor of visual-spatial memory component score when only the unilateral TL patients were considered? Was it simply due the differences in sample size, or is duration relatively more important for persons with TL epilepsy?
5. Do visual-spatial memory tests simply reflect how well persons process and remember novel stimuli (i.e., as opposed to more routinized stimuli)?
6. What are the similarities and differences between the Visual Naming subtest of the MAE and the BNT with respect to (1) sensitivity to left hemisphere and right hemisphere dysfunction, and (2) sensitivity to language dysfunction, visual-perceptual dysfunction, and general cognitive inefficiency?
7. How is performance on the BNT related to verbal skills versus general cognitive efficiency in normals and in particular patient groups?

Vita Auctoris

Margaret A. Newson was born on September 29, 1967, in Sudbury, Ontario. She grew up in Little Current, Manitoulin Island, where she attended Manitoulin Secondary School. She completed her final year of secondary school at F.E. Madill Secondary School, Wingham, Ontario, graduating in June 1986. In September 1986, she enrolled at Laurentian University where she completed one year of study. She subsquently transferred to the University of Toronto where she achieved a Bachelor of Science (Honours) degree in psychology in June 1990. Her honours thesis supervisor was Dr. Meredyth Daneman.

After completing her undergraduate degree, Margaret Newson was employed for two years as a research assistant at the University of Toronto under the direction of Drs. Mary Lou Smith and Morris Moscovitch. In September of 1992 she enrolled in the PhD programme in Clinical Neuropsychology at the University of Windsor. She obtained a Master of Arts degree in August 1994. Her thesis was supervised by Dr. Douglas Shore; Drs. Ged Namikas and Patricia Weir were on the committee. Finally, she defended her PhD dissertation on May 4, 1999. Her committee members were Drs. Douglas Shore, John Fisk, Patricia Weir, and Prof. Byron Rourke. The external-examiner was Dr. Marilyn Jones-Gotman of McGill University.

Margaret Newson married Dr. Geoffrey Haddock on May 8, 1993. They live in Exeter, England *met vier vissen*.